JUNE 27, 1953 PAGES 1261 TO 1318

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2
Telegrams: LANCET, RAND, LONDON **Telephone:** TEMPLE BAR 7228 and 7229

No. XXVI OF VOL. I, 1953
No. 6774 VOL. CCLXIV

LONDON, SATURDAY, JUNE 27, 1953
Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper

Pp. 120—Price 1s.
Annual Subscription: £2 2s.

'SONERYL' Trade Mark THE ORIGINAL BUTOBARBITONE

manufactured by MAY & BAKER LTD

distributors: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD., DAGENHAM

DISABILITIES
AND HOW TO LIVE WITH THEM
by 55 Patients
Demy 8vo 252 pages Price 10s. 6d. net, plus 6d. postage

"As men and women G.P.s will gain much from reading these stories; as doctors they will be in a better position to transmit to their patients some of the courage displayed by those anonymous authors. An altogether admirable book."—*Medical World.*
The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

CAREERS IN MEDICINE
Edited by P. O. WILLIAMS, M.A. (Cantab), M.B., B.Chir., M.R.C.P.
With contributions from 49 eminent medical authorities
Cr. 8vo 292 pages Price 15s. net, plus 8d. postage
This book outlines the particular qualities of mind, the type and amount of specialised training, required in each branch of the Medical Profession.
"... it should be in the hands of everyone who has to advise medical students, and certainly should be consulted by every newly-qualified doctor."—*The Practitioner.*
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Third Edition Now available
INTRODUCTION TO
DISEASES OF THE CHEST
By JAMES MAXWELL, M.D.(Lond.), F.R.C.P.(Lond.)
Physician, Royal Chest Hospital; Physician to the Ministry's Mass X-ray Unit; Consulting Physician, Royal National Sanatorium, Bournemouth; late Physician, St. Bartholomew's Hospital
Demy 8vo 308 + xii 66 Half-tone Illustrations
12s. 6d. net, plus 8d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

FANCONI & WALLGREN'S
TEXTBOOK OF PÆDIATRICS
English Edition edited by W. R. F. COLLIS, M.A., M.D., F.R.C.P., F.R.C.P.I., D.P.H.
Translated from the German by E. KAWERAU, M.B., M.Sc., A.R.I.C.
Eight-page, illustrated brochure available upon request.
1124 pages 440 illustrations 19 colour plates £7 7s. net
Wm. Heinemann Medical Books Ltd., Gt. Russell-street, W.C.1

THE LAW AND ETHICS OF DENTAL PRACTICE
By R. W. DURAND, M.R.C.S., L.R.C.P.
Formerly Secretary of the Medical Protection Society
and
D. MORGAN, L.D.S. (Leeds)
Formerly Deputy Dental Secretary of the British Dental Association
Foreword by Professor R. V. BRADLAW, M.D.S. Dunelm, F.D.S., M.R.C.S. Eng.
Professor of Oral Pathology, Durham University
Director, Newcastle-upon-Tyne Dental School
Expert guidance on the many problems which confront the dentist
Demy 8vo 98 + viii Price 7s. 6d. net, plus 4d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Fifth Edition Now available
PRINCIPLES OF MEDICAL STATISTICS
By A. BRADFORD HILL, D.Sc., Ph.D.
Demy 8vo 282 + x 10s. 6d. net, plus 6d. postage
With Twenty-five Exercises and Answers
The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

DISEASES OF THE NERVOUS SYSTEM
by Sir RUSSELL BRAIN, *D.M., P.R.C.P.*
'This book has become one of the most widely used and justly popular textbooks of neurology. The fourth edition is worthy of its predecessors.'—POSTGRADUATE MEDICAL JOURNAL.
FOURTH EDITION 1034 *pages* 85 *illustrations* 42s. *net*
OXFORD UNIVERSITY PRESS

The complete answer for macrocytic anæmias

Clinical experience over a decade has established that the administration of Anahæmin constitutes the most effective form of treatment for pernicious anæmia.

Anahæmin produces, with small and comparatively infrequent doses, a prompt and satisfactory erythropoiesis in patients in relapse, it ensures the maintenance of a normal erythrocyte level in patients in remission and is effective in preventing the onset of subacute combined degeneration of the cord.

Anahæmin has also been found to be of value in the treatment of herpes zoster and post-herpetic neuralgia. The suggested dosage is 4 ml. on alternate days until relief is obtained.

'ANAHÆMIN'

Anahæmin is available in :

1 ml. ampoules, Boxes of 3 at 8/3, 6 at 15/3, 25 at 58/6

2 ml. ampoules, Boxes of 3 at 13/6, 6 at 25/9, 25 at 100/-

Vials of 10 ml. at 19/10 and 25 ml. at 48/5.

Prices in Great Britain to the Medical Profession

Literature and specimen packings are available to members of the Medical Profession on request to the Medical Department

THE BRITISH DRUG HOUSES LTD. LONDON N.1

ANAH/E/117

JUNE 27, 1953 PAGES 1261 TO 1318

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6774 LONDON: SATURDAY, JUNE 27, 1953 CCLXIV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Headache and Hypertension — I. McD. G. Stewart, M.R.C.P. 1261
Intra-arterial Transfusion — D. G. Melrose, B.M.; A. O. Wilson, M.B. 1266
Poliomyelitis Following Inoculation — Dennis Geffen, M.D.; J. Hamilton Paterson, M.R.C.P.; S. M. Tracy, M.R.C.S. 1268
A Method of Treatment for Varicose Veins — M. G. Wilson, F.R.C.S. 1273
Assessment of Adrenocortical Activity by Assay of 17-Ketogenic Steroids in Urine — J. K. Norymberski, DR. ING.; R. D. Stubbs; H. F. West, M.R.C.P. 1276
Thiouracil in Pregnancy — Norah Elphinstone, M.B. 1281
Transient Hypothyroidism in a Newborn Infant — David Morris, M.R.C.P. 1284
The Radio-electrophysiologogram — C. S. Parker, M.D.; C. C. Breakell, L.D.S.; F. Christopherson 1285

SPECIAL ARTICLES

Controlled Hypotension in Anæsthesia — L. J. Hampton, M.D.; D. M. Little, JUN., M.D. 1299
The Practitioner in the N.H.S. .. 1300

PUBLIC HEALTH

Food-poisoning Caused by *Salmonella dublin* — A. M. McCall, M.R.C.S. 1302
Food-poisoning in Lancashire .. 1304
Lining a Reservoir 1305

MEDICAL SOCIETIES

Royal Society of Medicine: Medical Problems in Korea .. 1288

LEADING ARTICLES

Cardiac Catheterisation 1291
Nursing Problems in the Provinces 1292
Treatment of Renal Tuberculosis 1293

ANNOTATIONS

Comfortable Childbirth 1294
Vegetable Juices 1295
Chemotherapy of Actinomycosis 1296
Colonial Health Services 1296
The Lister Institute 1297
Ménière's Disease 1297
Hallux Valgus 1298
Spontaneous Pneumothorax 1298

LETTERS TO THE EDITOR

One-stage Prothrombin-time Test (Prof. A. J. Quick, M.D.) 1307
Treatment of Hypertension (Dr. G. L. Maison) 1308
Poliomyelitis (Dr. Oskar Turgel) 1308
Anticoagulant Drugs (Dr. Berton Lattin) 1309
The Nurse's Responsibility (Mr. Ellison Nash, F.R.C.S.) 1309
Immediate Results of Sanatorium Treatment (Dr. W. E. Snell) 1309
Medical History of the Second World War (Major-General G. E. MacAlevey, M.R.C.S.) ... 1310
Observations on Peptic Ulcer (Dr. Alan McGlashan) 1310
Hospital Costing (Dr. A. F. Mohun; Dr. F. Avery Jones) 1311
Injuries of Spinal Cord (Dr. James Burnet) 1312
Prevention of Postoperative Chest Complications (Dr. J. Kohn, Dr. M. Vitali) 1312
Junior Hospital Staffing (Dr. K. Cobban) 1313
Localised Muscular Atrophy in Diabetes (Dr. Cedric Hirson) 1313
Troublesome Tapeworms (Dr. E. Frankl) 1313
Bread (Dr. K. E. Barlow; Dr. Z. A. Leitner) 1313
Relief of Mental Hospitals (Dr. J. W. Mullner) 1314
The Illegible Candidate (Dr. George Graham; Dr. Robert Coope) 1314
Trichomonas Vaginitis (Dr. J. L. Patton) 1315
Tuberculosis in Glasgow (Dr. Hugh Paul) 1315

REVIEWS

Notices of Books 1289

PARLIAMENT

Question Time 1305

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents .. 1306

OBITUARY

Andrew John Metford Wright .. 1315
Albert Edward Evans 1315
Herbert Bertram 1316
Dame Georgiana Buller 1316

NOTES AND NEWS

Requirements for the D.P.M. .. 1316
Saving Money on Hospital Laundries 1316
Ambulance Services 1316
Royal Society of Tropical Medicine and Hygiene 1317
Medical Sickness Society 1317
Universities of the Commonwealth 1317
Anthropological Solutions for Paternity Problems 1317
Transplantation Bulletin 1317
Light-weight Crutches 1317
The Rat 1317

University of Leeds 1317
University of Sheffield 1318
Royal College of Surgeons in Ireland 1318
Irish Conjoint Board 1318

Diary of the Week 1318
Appointments 1318
Births, Marriages, and Deaths .. 1316

for prolonged therapy . . .

'MIXTAMYCIN'

brand

streptomycin plus dihydrostreptomycin

. . . with reduced ototoxicity

Distributed by:

ALLEN & HANBURYS LTD. BRITISH DRUG HOUSES LTD. BURROUGHS WELLCOME & CO.
EVANS MEDICAL SUPPLIES LTD. IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD.
PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD.

Manufactured by:

THE DISTILLERS COMPANY (BIOCHEMICALS) LIMITED

Owners of the trademark 'Mixtamycin'

Bioglan

VITA-E 75 I.U.

GELUCAPS

(Vitamin E)

in the treatment of

Cardiovascular-Renal Diseases

after the method used at the Shute Institute for Clinical and Laboratory Medicine, Canada.

Each Gelucap contains a concentrate of natural esters (d,alpha-tocopherol acetate) from vegetable oils, type VI, equivalent to 75 mgm, d.l. alpha-tocopheryl acetate.

This therapy is today extensively prescribed in the U.K.

Sole Manufacturers:

THE BIOGLAN LABORATORIES LTD., HERTFORD, HERTS.

Tel. Address: "BIOGLAN TOLMERS" *Literature on request* Phone: CUFFLEY 2137

Nutrition in Convalescence

It has been suggested that special attention should be paid to pre- and post-operative nutrition. During convalescence there may be an increased need for the essential nutrients and particular care should be taken to ensure that the patient receives an adequate supply of these.

In planning meals for the convalescent the protective foods are therefore important. Marmite yeast extract supplies essential B_2 vitamins and is especially useful in the convalescent diet, as it adds an appetising flavour to many dishes and can also be served as a drink.

MARMITE

yeast extract

Literature on request

contains

Riboflavin (vitamin B_2) 1·5 mg. per oz.

Niacin (nicotinic acid) 16·5 mg. per oz.

Obtainable from chemists and grocers

Special terms for packs for hospitals, welfare centres, and schools

5306 The Marmite Food Extract Co., Ltd., 35, Seething Lane, London. E.C.3

DISC LESIONS

for the General Practitioner

JAMES CYRIAX, M.D.

The first publication on disc lesions specially for the general practitioner and student. Dr. Cyriax deals with the type of case often dismissed as "fibrositis" or "rheumatism," whose treatment is generally as dull for the doctor as it is unrewarding for the patient.

From this small pamphlet the reader can learn how to assess the history, conduct the clinical examination, make a precise diagnosis and carry out effective treatment. Such discs as are not reducible by manipulation are given, together with indications for alternative treatment.

Demy 8vo. Paper, 5s.

CASSELL

Just published by The Year Book Publishers, Inc., Chicago, and soon available in this country:

THE PHYSICIAN IN ATOMIC DEFENSE

Atomic Principles, Biologic Reaction and Organization for Medical Defense

By T. P. SEARS, M.D., F.A.C.P.

Associate Clinical Professor of Medicine, University of Colorado School of Medicine

CONTENTS: Introduction. I. *Atomic Theory, Basic Physics and Atomic Bombs:* Atomic Structure. Radioactivity. Isotopes. Health Physics. Nuclear Fission. Chain Reaction, etc. Atomic Bombs, Phenomenology and Hazards of Atomic Bomb Bursts. II. *Clinical, Biological, Pathologic and Therapeutic Aspects:* Clinical Aspects. Clinical Syndromes of Radiation Sickness. Ionization and Biologic Reaction. Pathology of Total Body Irradiation. Management of Casualties. Instrumentation. III. *Organization of the Medical Department for Atomic Defense.*

1953 5½ x 8 308 pages 45s.

Distributed in the United Kingdom by

INTERSCIENCE PUBLISHERS, LTD.
2a Southampton Row London, W.C.1

THE MEDICAL ANNUAL

1953

Edited by
Sir HENRY TIDY, K.B.E.
and
A. RENDLE SHORT

With the collaboration of 45 *contributors*

71*st issue.* 5½ × 8¼ *in.* 494 *pp.* 72 *plates and* 29 *text illustrations.* **27s. 6d.**, *postage* **1s. 2d.**

There can be few medical practitioners who are not already familiar with the Annual, but we would once again remind you how essential it is to order a copy regularly each year in order to keep abreast of all the recent developments in medicine and surgery. The 71st issue of this indispensable medical companion and book of reference appears in a new dress in this the Coronation year. The typographical arrangement has been improved by the use of larger type of recent design, and elsewhere minor changes have been carried out to make the pages additionally attractive. Lastly, the familiar green cloth binding has been redesigned in a contemporary style.

JOHN WRIGHT & SONS LTD., BRISTOL

NEW BOOKS . . .

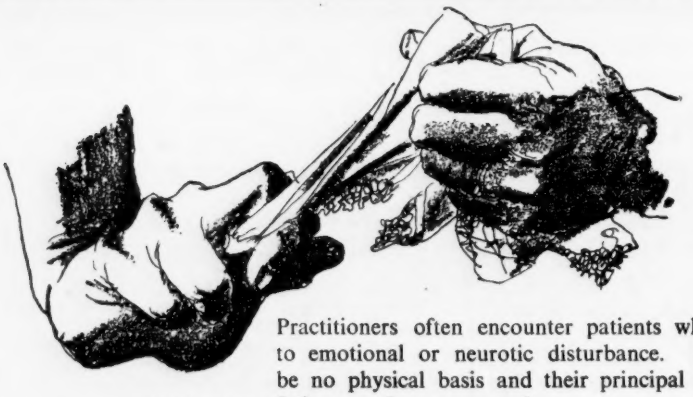
PATHOLOGY OF TUMOURS, Second Edition. *Just Published.* By R. A. WILLIS, D.Sc., M.D., F.R.C.P. The new edition of this famous standard work takes account of all recent developments in the subject. Pp. x + 997 + Index. 500 illustrations. Price **84s.** net.

MODERN TRENDS IN DIAGNOSTIC RADIOLOGY, Second Series. *Ready Shortly.* Edited by J. W. McLAREN, M.A., M.R.C.P., F.F.R., D.M.R.E. A new collection of articles describing emergent tendencies in technique, apparatus, etc., by a team of eminent authorities. Pp. xii + 394 + Index. 367 illustrations. Price **70s.** net.

MODERN TRENDS IN UROLOGY. *Now Ready.* Edited by E. W. RICHES, *M.C.*, M.S., F.R.C.S. This latest addition to the Modern Trends Series gives descriptions of modern treatment and the techniques of numerous operations including partial nephrectomy, renal transplantation and perineal prostatectomy. Pp. x + 462 + Index. 226 illustrations. Price **75s.** net.

A HANDBOOK ON CANCER FOR NURSES AND HEALTH VISITORS. *Ready June.* By RONALD W. RAVEN, *O.B.E.*(Mil.), F.R.C.S. This new book falls into three parts. Part I deals with general aspects of the subject, Part II describes the early symptoms of the disease in various parts of the body, with notes on treatment, and Part III deals with the care of the patient. Pp. viii + 95 + Index. 21 illustrations. Price **12s. 6d.** net, by post 7d. extra.

Butterworths, 88 Kingsway, W.C.2 (*Showroom: Bell Yard, Temple Bar, W.C.2*)



Nervous Exhaustion

Practitioners often encounter patients whose ill-health is due mainly to emotional or neurotic disturbance. Frequently there appears to be no physical basis and their principal symptoms are usually undue nervousness, fatigue and poor appetite.

For these mildly neurasthenic and exhausted cases 'BEPLETE' Wyeth is uniquely appropriate. It contains Phenobarbitone and Vitamin B-complex as an appetising Elixir, and so provides a quieting relaxation, while at the same time supplying nutritional factors known to be essential for the energy requirements of nervous metabolism.

'BEPLETE' contains:—
Phenobarbitone B.P. ¼gr.: Aneurine Hydrochloride 1.5 mg.: Riboflavin 1.0 mg.: Pyridoxine Hydrochloride 0.33 mg.: Nicotinamide B.P. 10.0 mg.: Pantothenyl Alcohol 0.2 mg. (equivalent to 0.212 mg. Pantothenic Acid): Alcohol 15%.

'Beplete'
Trade Mark

John Wyeth & Brother Limited, Clifton House, Euston Road, London, N.W.1. Wyeth

A vitamin prescription suitable

for patients of all ages . . . . .

Vitavel Syrup is exceptional, not only in containing vitamin B_1 in addition to vitamins A, C and D, but in being completely miscible with water and having no suggestion of taste or smell of fish oil.

It can be taken undiluted or in water or soda water. Makes the ideal drink for the febrile or debilitated patient.

VITAVEL *Syrup*

The principal vitamins in a palatable orange base

VITAMIN A · VITAMIN B_1 · VITAMIN C · VITAMIN D

Available in bottles of
6 *fl. oz.* **3/9**
40 *fl. oz.* **21/-** *less usual professional discount.*

Each fluid ounce contains at time of manufacture

VITAMIN A . . . 20,000 i.u	VITAMIN C . . . . 80 mg.
VITAMIN B_1 . . . **4.0 mg.**	VITAMIN D . . . 3,000 i.u

Clinical sample and literature on request to:-

VITAMINS LIMITED (DEPT. B.92), UPPER MALL, LONDON W.6

GLANOID

Tryptar

PURIFIED CRYSTALLINE TRYPSIN

For Physiologic Debridement of Necrotic Tissue, Thoracic Empyema, Burn Eschars, Infected Surface Lesions.

Evidence is accumulating from Clinical Trials Confirming the Value of Tryptar in these conditions.

AVAILABLE TO HOSPITALS ONLY

Write for Literature to :—

THE ARMOUR LABORATORIES

(ARMOUR & COMPANY LTD)

LINDSEY STREET, LONDON, E.C.1

Telephone : CLERKENWELL 9011

Telegrams : "ARMOSATA-PHONE" LONDON

*A **new** approach to 'khellinisation'*

KHELLANALS

suppositories 'Pabyrn'

Khellin therapy without nausea

A non-toxic form of pure khellin providing effective treatment in chronic bronchitis, bronchial asthma, angina pectoris, renal colic — without the distressing side-effects so common to parenteral and oral administration.

Clinical sample and literature on request

PAINES & BYRNE LTD., Pabyrn Laboratories, Greenford

Telegrams : GLANDS, GREENFORD Telephones : PERIVALE 1143 (5 lines)

EPHAZONE tablets

Rational, symptomatic treatment in
ASTHMA AND BRONCHITIS

Each tablet contains Ephedrine, the important anti-spasmodic for bronchial spasm, Theobromine, for its relaxing effect on the bronchial muscle and for stimulation of the coronary circulation, Phenazone, for its soothing effect on the higher centres, and Calcium gluconate, a readily absorbable calcium salt, for diminishing capillary permeability and checking the secretion of mucus.

These active ingredients with complementary effects in bronchial asthma are presented in the following proportions in the 'EPHAZONE' Tablet:

Ephedrine hydrochloride - - ¼ grain
Theobromine - - - - - - ½ grain
Phenazone - - - - - - - 1 grain
Calcium gluconate - - - - ¼ grain

This preparation is sanctioned for prescription under N.H.S.

Please write for samples and descriptive leaflet

EPHAZONE LTD
59 BROOK ST., LONDON, W.1
TEL: MAYFAIR 5496

E.1

Kaylene-ol

the satisfactory and palatable emulsoid of kaolin and liquid paraffin

There is no more "physiological" preparation for routine use:—

(a) As a gentle laxative at bedtime. It is effective when stimulant purgatives often fail. This is especially so in the face of colon spasm and hypertonia.

(b) As a preventive of dyspepsia, when it should be taken some few minutes before every meal.

Samples and literature on request

KAYLENE **LIMITED**

Sole Distributors: **ADSORBENTS, LTD.**, WATERLOO RD., LONDON, N.W.2

6

Elastoplast Porous Adhesive Bandages are now prescribable on Form E.C.10 from July 1st

The adhesive mass of Elastoplast is now rendered porous by a special process. The bandage with the Porous Adhesive has all the advantages associated with Elastoplast—firm adhesion, compression and support—while permitting free evaporation of sweat. The price is unchanged.

When prescribing Elastoplast, add " Porous Adhesive " to your script. Full details from Medical Division, T. J. Smith & Nephew Ltd., Hull.

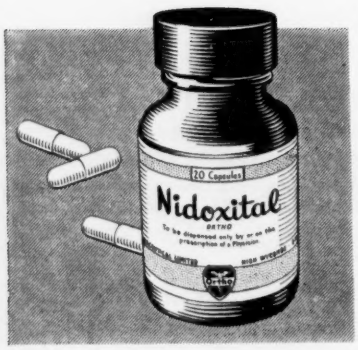
Outside the British Commonwealth Elastoplast is known as Tensoplast.

Elastoplast
TRADE MARK

POROUS ADHESIVE BANDAGES

Bright and early

for your pregnant patients with nausea and vomiting



Nidoxital

gives rapid and prolonged relief

For full-range therapeutic and prophylactic control of the complex problem, Nidoxital provides five effective agents :

Benzocaine—to diminish gastric excitability

Nicotinamide—to reduce excessive peristalsis

Pentobarbital sodium—to depress central excitability

dl-Methionine—to support normal liver function

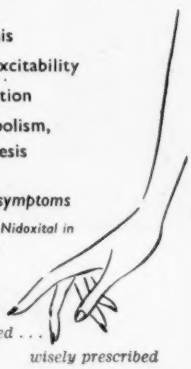
Pyridoxine—for fatty acid and protein metabolism, maintenance of nerve function and erythropoiesis

In almost all patients treated with Nidoxital, symptoms disappear within one to three days — "The Use of Nidoxital in Emesis Gravidarum" (Am. J. Obst. & Gynec. 59: 458, 1950)

Nidoxital in bottles of 12, 20 and 100 capsules. 20 capsules are usually sufficient for complete control.

Dosage : One capsule 30 to 45 minutes before meals in the usual case, increased to 2 to 3 capsules in exceptionally severe cases.

LITERATURE ON REQUEST



widely indicated . . .
wisely prescribed

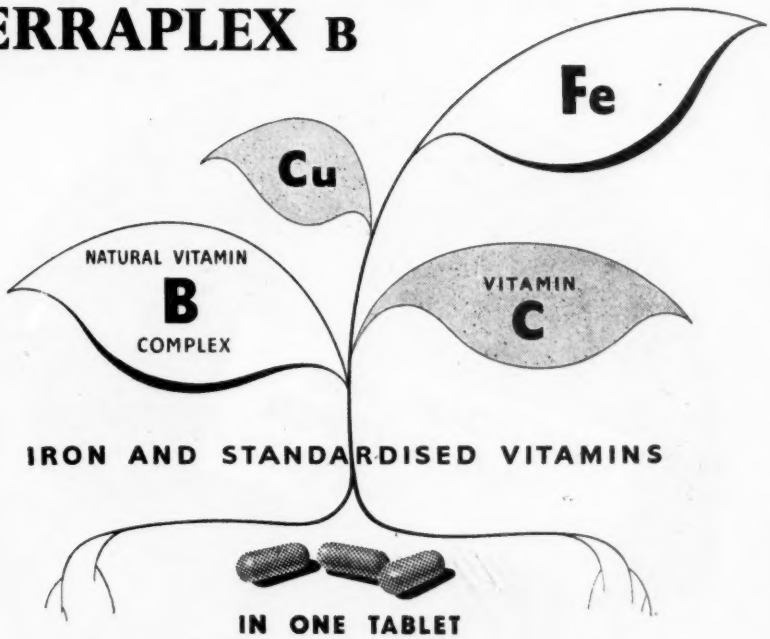
Ortho *Pharmaceutical Limited*

HIGH WYCOMBE · BUCKINGHAMSHIRE · ENGLAND

Makers of Gynaecic Pharmaceuticals

Ortho

FERRAPLEX B



ADVANTAGES

* FERRAPLEX B, by combining adequate iron dosage with standardised vitamin content, provides a comprehensive and efficient hæmatinic compound for routine use, particularly in pregnant and under-nourished women, in adolescence, in hæmorrhagic conditions and in the debility of advancing age.
* In recent years it has been shown that simultaneous administration of vitamin C and the B complex group together with iron gives much better results in hypochromic anæmias. The natural vitamin B complex used in FERRAPLEX B is a concentrate prepared from brewers' yeast.
* The comprehensive "one tablet" formula, the *standardised* vitamin potency and the reasonable price of FERRAPLEX B entirely conform with current economic requirements.

COMPOSITION

The average daily dose of six FERRAPLEX B tablets contains:—

FERROUS SULPHATE .....1 gramme
COPPER CARBONATE.....2 mg.
ASCORBIC ACID (Vitamin C)....50 mg.
NATURAL VITAMIN B COMPLEX .....2 grammes

including

Aneurine hydrochlor. (B_1).....3 mg.
Riboflavine (B_2).....6 mg.
Nicotinamide .....30 mg.
Pantothenic acid .....480 µg.
Pyridoxine (B_6) .....160 µg.
and folic acid, choline, inositol, biotin, para-aminobenzoic acid and other naturally occurring factors of the vitamin B complex.

PACKINGS AND PRICES. FERRAPLEX B tablets are available in bottles of 50 at 5/3d. and 250 at 23/3d. Retail prices subject to Professional discounts.

FERRAPLEX B

is manufactured in the laboratories of C. L. BENCARD LTD

GREAT WEST ROAD, BRENTFORD, MIDDLESEX

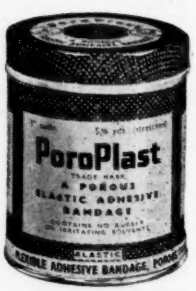
PoroPlast

TRADE MARK

Research during the past ten years into skin irritation associated with the use of adhesive plaster has resulted in notable improvements over the old type of elastic adhesive bandage.

PoroPlast contains no rubber, and it is entirely free from the irritating solvents and resins usually embodied in elastic adhesive bandages. PoroPlast is porous over its whole surface, giving ventilation *even where two layers overlap*. It offers greatly increased plaster toleration even on the most sensitive skins. Samples on application.

N.H.S. *PoroPlast conforms to the Specification for Flexible Adhesive Bandages Porous of the Drug Tariff (April 1953 Amendment) and is freely prescribable in widths 2½ in. and 3 in. on E.C.10 from 1st July, 1953, under the name "PoroPlast."*



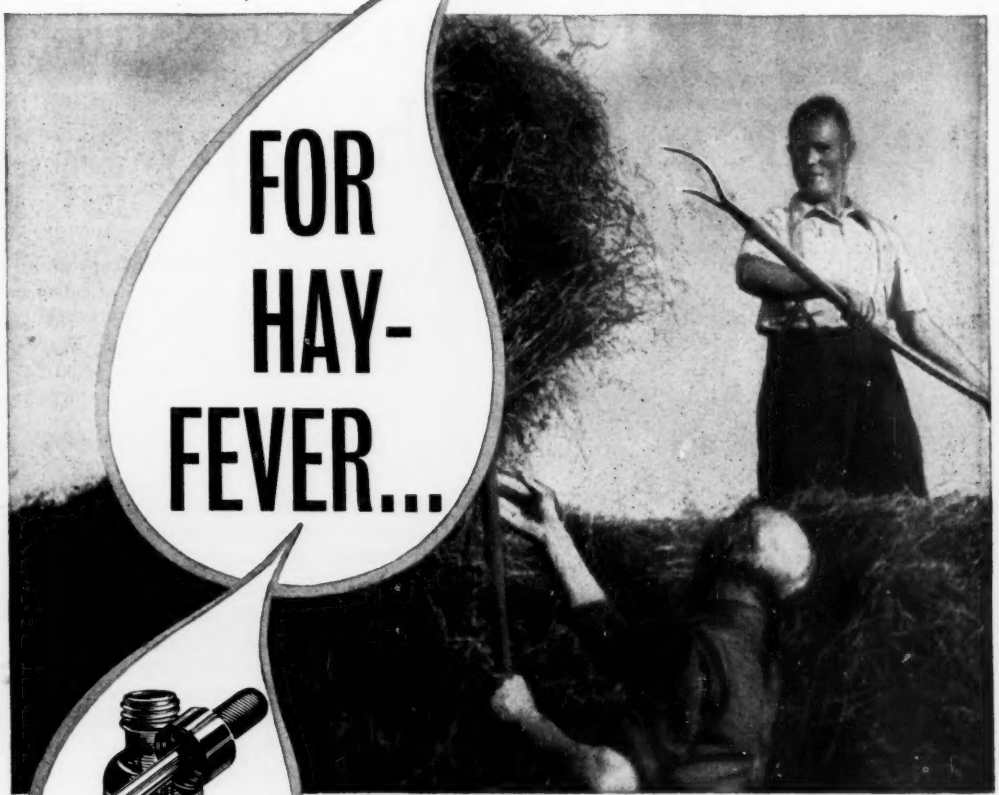
PoroPlast

POROUS ELASTIC ADHESIVE BANDAGE

(Flexible Adhesive Bandage, Porous, Drug Tariff)

THE SCHOLL MFG. CO. LTD., 182-204, ST. JOHN STREET, LONDON, E.C.1

FOR HAY-FEVER...



THE CONTROL of hay-fever still remains a problem, but whatever therapy is adopted the additional use of a nasal decongestant is invaluable.

FENOX, by virtue of its unique properties, is the ideal preparation for both children and adults, **giving immediate and prolonged relief without . . .**

irritation of inflamed mucosa
impairment of ciliary action
undesirable side-effects

FENOX is water-miscible and non-oily. It has the same viscosity as mucus and remains at the site of action.

FENOX—*Isotonic Nasal Drops of Phenylephrine and Naphazoline*
Supplied in ½ fl. oz. dropper bottles

May be prescribed on Form E.C.10. Basic N.H.S. price 1/8d.

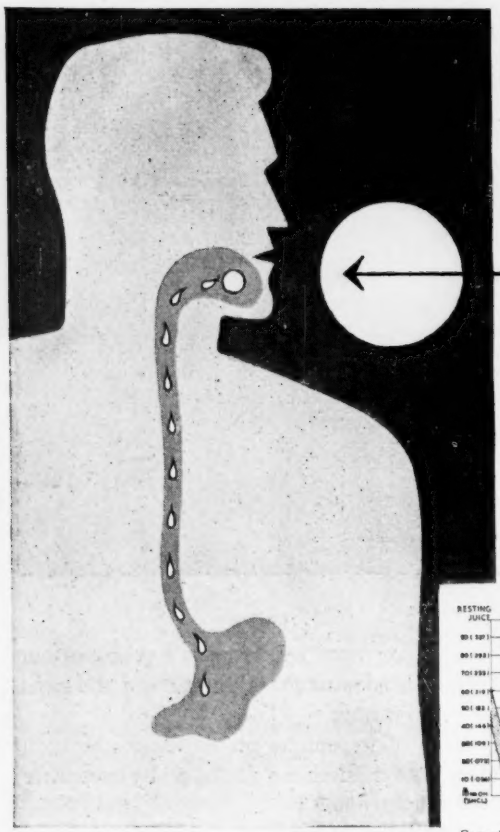
FENOX
NASAL DROPS

BOOTS PURE DRUG COMPANY LIMITED
STATION STREET NOTTINGHAM

Boots
SI55B

11

The key to successful peptic ulcer therapy



WHENEVER continuous neutralization of gastric acidity is required—in active and quiescent peptic ulcer, gastritis, hyperacidity—NULACIN TABLETS are indicated.

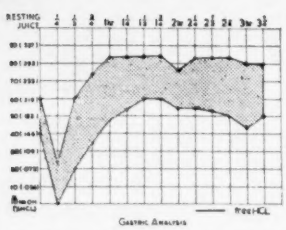
The successful clinical behaviour of NULACIN TABLETS is accounted for by their composition and unique manner of use.

Dosage

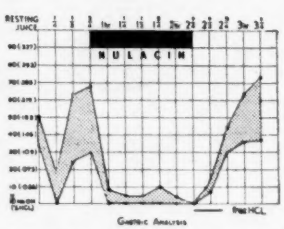
Beginning half-an-hour after food a NULACIN TABLET should be placed in the mouth between the cheek and the gum and allowed to dissolve.

During the stage of ulcer activity up to three tablets an hour may be required. For follow-up treatment the suggested dosage is one or two tablets between meals.

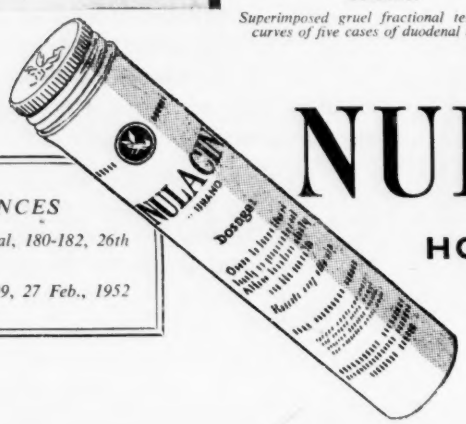
NULACIN TABLETS are not advertised to the public and there is no B.P. equivalent. NULACIN is supplied in tubes of 25 and 12 tablets. The dispensing pack of 25 tablets is free of Purchase Tax.



Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer



Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.



REFERENCES

British Medical Journal, 180-182, 26th July, 1952.

Medical Press, 195-199, 27 Feb., 1952

NULACIN

HORLICKS LIMITED

Pharmaceutical Division

SLOUGH · BUCKS

For wide-range choice

of administrative forms...

Every recognized and commonly used means of PAS administration is made available through one or other of the various forms of 'Aminacyl' brand of Calcium PAS or of Sodium PAS B.P.C.

Cachets

Cryst. Ca or Na PAS: 1.5 gm., 100's and 500's; 2.0 gm., 80's and 400's.

Granulate

Cryst. Ca PAS: 100 gm., 400 gm., 2,000 gm. packs.

Dragées

Cryst. Ca or Na PAS: 0.4 gm., 0.5 gm., 0.75 gm., 250's and 1,000's.

Dry Ampoules

1 and 6 x 2.41 gm. crystal.=2.0 gm. Na PAS anhyd.

Solution Ampoules

Na PAS: 20% topical; 2.8% (isotonic) ophthalmic.

Bulk Powder

Cryst. Ca or Na PAS: 100 gm., ¼, ½, 1 and 5 kg.

Intravenous

Purified crystalline Na PAS for I.V. solutions; bottle of 250 gm.

Further information from the Medical Dept.,
A. WANDER LIMITED,
42 Upper Grosvenor Street,
Grosvenor Square, London W.1.

CANADA: A. Wander Ltd., Peterborough, Ontario.
AUSTRALIA: A. Wander Ltd., Devonport, Tasmania.
NEW ZEALAND: A. Wander Ltd., Christchurch.
INDIA: Grahams Trading Co. (India) Ltd., 16 Bank Street, Bombay.
PAKISTAN: Grahams Trading Co. (Pakistan) Ltd., P.O. Box 30, Karachi.
CEYLON: A. Baur & Co. Ltd., Colombo.

M.374

'SULPHAMEZATHINE'

Sulphadimidine B.P. Trade Mark

'SULPHAMEZATHINE' was included in the medical equipment of the British Everest Expedition because it provides the optimum requirements of sulphonamide therapy, namely efficiency, reliability and safety under all conditions. To all members of the expedition we express our admiration of the skill, endurance and daring displayed in their magnificent achievement, typical of the British tradition.

Other I.C.(P) drugs included :

ANTIBIOTICS :
'Avloprocil' N.A. Procaine Penicillin Injection Fortified.
Crystalline Penicillin G 'Avlon' brand

ANTIMALARIALS :
'Paludrine' Proguanil Hydrochloride

OTHER SULPHONAMIDES :
Sulphaguanidine 'Avlon' brand

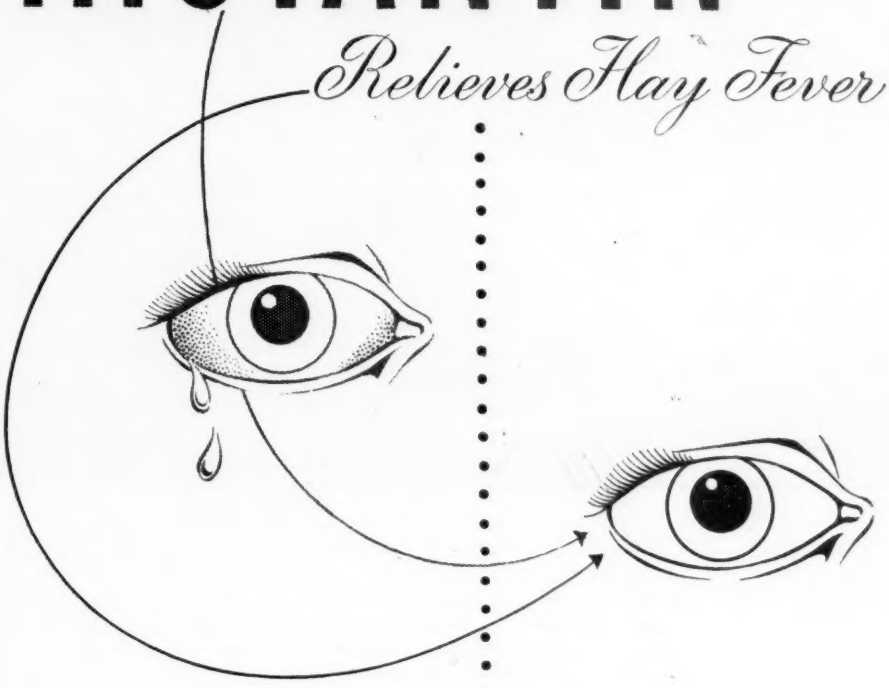
IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED

A subsidiary company of Imperial Chemical Industries Limited **Wilmslow, Manchester**

Ph.376

'HISTANTIN'

Relieves Hay Fever



'HISTANTIN' BRAND

Chlorcyclizine Hydrochloride

Designed for fewer side effects, 'Histantin' is of proven value in the symptomatic management of hay fever. A single daily dose of this antihistamine is sufficient to keep most patients free from symptoms. 'Histantin' is available as 50 mgm. compressed products in bottles of 25, 100 and 500.

BURROUGHS WELLCOME & CO. *(The Wellcome Foundation Ltd.)* LONDON

*CC

"I dread the rustling of the grass"

WILLIAM WORDSWORTH

No sooner has the blossom languished
and spring shed her coat of many
colours than the tall grasses ripen. The air is
again pollen-laden. To those who love the countryside
these richly-clothed meadows are a joy: to
sufferers from hay-fever they are
merely the signal for a fresh period of acute discomfort.
Yet there is a solution — BENADRYL,
probably one of the most potent of all histamine antagonists,
may be taken just before and during the
pollen seasons and, in the majority of cases,
provides effective relief.

BENADRYL a successful anti-histamine

Capsules (25 or 50 mg.) in bottles of 50 & 500;
Elixir in bottles of 4 & 16 fl. ozs.

PARKE, DAVIS & Company, Limited *Inc. U.S.A.* Hounslow, Middlesex Telephone: Hounslow 2361

262

HEADACHE AND HYPERTENSION

I. McD. G. STEWART
M.D. Lond., M.R.C.P.

SENIOR MEDICAL REGISTRAR, UNITED BRISTOL HOSPITALS; TUTOR IN MEDICINE, UNIVERSITY OF BRISTOL

IN recent years fresh efforts have been made to treat hypertension by arbitrary reduction of the blood-pressure; and indeed with some success. By sympathectomy, or treatment with drugs, not only has it proved possible to lower the pressure, at least temporarily, but also left ventricular failure has been observed to recover, heart size to diminish, fundal changes to regress, and electrocardiographic abnormalities to return to normal. At the same time paroxysmal breathlessness has been overcome and vision improved. These are substantial benefits. Unfortunately they are seldom achieved. Many claims to success have been based upon less substantial grounds. They have derived solely from the alleged cure of symptoms. But of what, exactly, had these patients complained? What are these "symptoms of hypertension"? Do they indeed exist apart from those disorders of organs which accompany or complicate the course of hypertensive disease?

Clearly some doctors believe that they do. The most highly accredited symptom is "headache." Others widely acknowledged include "dizziness," "lack of energy," and "lack of concentration." The cure of such complaints has often been taken to prove the worth of a treatment. More than one remedy has claimed support solely on the strength of its reputed efficacy in the "relief of symptoms"—the particular ills so ameliorated remaining unspecified.

This kind of language has appeared repeatedly in the medical literature during the past few years. Even Smithwick (1940), who first popularised splanchnic sympathectomy, scarcely defined the "symptomatic relief" which he designated one of the important objects of surgery; admittedly his main intent was to offer an improvement in survival-rate. Many of his followers have been less restrained.

For example, no misgiving prevented FitzGerald (1950) from proclaiming his view that "symptomatic relief is one of the greatest blessings conferred by sympathectomy . . . symptoms determine the operability . . . one frequently operates for their alleviation alone. This is a simple but well-proven maxim." He did not define these symptoms. His contention, in common with that originally put forward by Smithwick (1948), was that operation should be undertaken early. Clearly, therefore, they could not have been caused by heart-failure, uræmia, or hypertensive retinopathy: such are late events in the disease.

"Shortness of breath, intellectual decline, and irascibility" were said by Atkins (1950) to have been evident among his hypertensive patients, many of whom, nevertheless, "complained mainly of headache." Hammarström and Bechgaard (1950) defined a group of hypertensives in whom there were "marked subjective symptoms but without signs of myocardial damage"; on the strength of this criterion these hypertensives were subjected to surgery. Yet the symptoms thus held to have been so significant could scarcely have included paroxysmal dyspnœa or visual disability, since pulmonary œdema consequent on hypertension, and retinal changes sufficient to affect vision, are, again, virtually always accompanied by the appearances of myocardial strain or failure.

Chris (1951) accepted "severe headaches" as one of the most important of "definite symptoms referable to hypertension," thereby constituting an indication for sympathectomy. Allen (1952), however, has reported that American surgeons have recently lost some of their enthusiasm for sympathectomy as a means of dealing with "hypertensive headache."

Most of the physicians who have conducted trials with the new methonium drugs have written in similar vein.

Thus Murphy (1951) reported that "symptomatic improvement . . . was impressive" in most of his cases, while Mackey and Shaw (1951) maintained that "of all the manifestations of hypertension headache is the most easily relieved."

Smirk and Alstad (1951) were satisfied about the benefit to "headache, dyspnœa, and vertigo." A few months later Smirk (1952) gave as the main hope offered by prolongation of the action of hypotensive drugs the prospect that "more relief might be afforded to the 10% of hypertensive patients whose headaches are at present insufficiently relieved."

Much the same type of claim has been advanced on behalf of the rice-diet treatment originally suggested by Kempner. A report published by a committee of the Medical Research Council (1950) included the sentence: "Of 33 patients with symptoms referable to hypertension 25 (75%) obtained relief. Headaches, which were present in 26, disappeared in all but 4, often within a few days of starting the diet."

It cannot be denied that people who have hypertension are liable to complain of headache, to experience dizziness and shortness of breath, even to lose their tempers. Such distresses, however, are not unusual. It does not follow that the blood-pressure is in any way to blame. To establish a sequence of cause and effect more evidence is required. Can there be demonstrated any clear relation with hypertension? Is there, perhaps, a type of headache that is characteristic of hypertensive disease?

Despite the confident assertions that have been quoted these are disputed questions:

For example, Russell Brain (1952) writes: "High blood-pressure causes paroxysmal, throbbing, or 'bursting' headaches," and Platt (1950) asserts that "true hypertensive headache may be frontal or occipital and is usually most prominent in the early morning." Alexander (1948), in common with many other writers, has drawn attention to a parallel with migraine.

Symonds (1946), however, contents himself with the more cautious statement that "headache is a common but inconstant symptom of arterial hypertension," while making the reservation that he is excluding from consideration the "relatively rare condition known as hypertensive encephalopathy." Wood (1950a) goes further and declares roundly that "it is doubtful whether any symptoms can be ascribed to high blood-pressure itself." Others have agreed with this view.

It was in an attempt to clarify this association between high blood-pressure and the symptoms that so often accompany it that the following clinical study was undertaken. Particular attention was paid to the significance of headache.

Scheme of Investigation

The study was made upon 200 consecutive cases of severe hypertension and upon a number of controls. All the patients were interviewed and examined by me. Among the hypertensives the only criterion of selection was the height of the diastolic blood-pressure. The standard adopted was a minimum of 120 mm. Hg, measured with the patient recumbent, after ten minutes' rest in that position. Whenever a reading had been made previously by another observer, the level then noted had nearly always been considerably higher than that obtained by this routine technique. Occasionally the pressure was found at a subsequent examination to have fallen below 120 mm. Hg. Unless there had been obvious cause for this—e.g., intervening cardiac infarction—all record of the patient was expunged from the survey. It was thought best to abide by the blood-pressure alone as a standard for inclusion in the series. Inevitably, however, this led to the omission of a few patients who, though clearly severely hypertensive, never presented a sufficiently high diastolic level, because when they were first seen, they had cardiac failure, recent infarction, or some similar complication.

The following points were determined:

(1) Whether or not the patient was aware of the raised blood-pressure.

(2) The volunteered symptoms, if any, in the order in which they were volunteered.

(3) The presence or absence of headache, whether volunteered or elicited.

(4) The nature of any headache admitted—in particular, its site and distribution, how long suffered in its present form, any previous migraine or tendency to have been a "headachy person," whether the pain was tending to get better or worse, its character, its duration, any precipitating or relieving factor, any history of past head injury, and any other possible cause of headache apart from hypertension.

(5) The patient's age on first interview, age on identification as hypertensive, present blood-pressure, cardiac rhythm, retinal appearances, electrocardiograms, and left ventricular size estimated radioscopically.

In pursuing these inquiries care was taken to avoid suggestion. Many patients began at once, early in the first consultation, to talk spontaneously of their "blood-pressure." If they did so, the subject was at this stage brushed aside. Instead they were asked what had first induced them to visit their own doctor, and whether they had now any symptoms. Later the blood-pressure was taken. At this point, if the patient had so far said nothing to show that he was already aware of his condition, his attention would be drawn to the sphygmomanometer. As if the aim were to make conversation, a casual question would be put asking whether he had "ever seen one of these things before." Sometimes the answer would be crisply to the effect that he had seen one only too often, ever since they had found out about his "blood-pressure." On the other hand, there might be no flash of recognition, the reply coming only in vague terms such as: "Isn't it the thing you take blood-pressures with?" Exchanges of this kind invariably provided the clue to the patient's knowledge or ignorance of his hypertension without telling him anything, and without, apparently, evoking his curiosity.

A similar care was exercised in seeking to elicit the symptom of headache if it were not volunteered. Thus, for instance, the only spontaneous complaint might be of pain in the chest. If nothing more were forthcoming, there would then be addressed to the patient some such seemingly routine question as this: "You're all right in every other way, I suppose—no reason why you shouldn't be. You've not lost any weight? No cough? Or headache? No pains in the legs?" If the word "headache" were seized on, that was taken as evidence of the presence of this symptom on elicitation. Before its acceptance as significant it was further pointed out that, of course, everyone gets headaches from time to time; the present concern was only with something definite.

Findings

Of the 200 hypertensives 93 were men and 107 women. The average diastolic pressure of the whole series was 136 mm. Hg. All but 5 were in normal rhythm. Headache was volunteered by 57 patients, with men and women in about equal proportion; two-thirds of these women were of menopausal age. The average diastolic pressure of all those volunteering headache was 145·5 mm. Hg. From a further 31 patients the symptom was elicited. Thus the total number of patients laying claim to headache was 88; leaving 112 unaffected in this way. Further investigation was made into factors which, it was thought, might throw light on the relationship between such headache, or its absence, and the hypertension.

SEVERITY OF HYPERTENSION

The standards of severity adopted were four—the height of the diastolic pressure, the retinal appearances judged by the grading of Keith et al. (1939), the electrocardiograms, and the size of the left ventricle estimated on radioscopy. The interpretations that may be put on abnormalities presenting in these last two investigations are, of course, often highly debatable. In this survey only unequivocal electrocardiographic changes, for which hypertensive "strain" seemed overwhelmingly the most likely cause, were accepted as significant.

TABLE I—RELATION BETWEEN PRESENCE OF HEADACHE AND SEVERITY OF HYPERTENSION

Category	No. of patients	Average diastolic B.P. (mm. Hg)	E.C.G. indications of L.V. strain	Fundi of hypertensive grade II or more	Hypertensive L.V. change on radioscopy
Headache ..	88	140·8	52%	51%	78%
No headache	112	133·6	69%	36%	60%

Patients with and without headache were compared (see table I). This shows that the average diastolic pressures of the two main groups were fairly close to each other, being respectively 140·8 and 133·6 mm. Hg. In both groups the scatter was wide. Thus 3 of the 4 highest values in the whole series, all higher than 180 mm. Hg, were found in patients who would admit to no headache. Of the other indications of severity radioscopic enlargement of the left ventricle favoured the group with headache, although not very much. By contrast electrocardiographic changes were seen slightly more often in the group with no headache. These differences were insignificant. Relative diminution in the calibre of the retinal arteries did, however, show an apparently significant tendency to be more severe in the patients with headache—51% against 36%. Moreover, as Pickering (1942) has found, the diastolic pressure tended to be highest among the patients with papill-œdema—the criterion of so-called "malignant" disease. There were 18 such patients. Their average diastolic pressure was 159 mm. Hg. Of these, 11 had headache. Apart from this it was at once evident that the severity of the hypertension gave no indication as to whether or not any individual patient might complain of headache.

TABLE II—RELATION OF HEADACHE TO KNOWLEDGE OF HYPERTENSION WITHIN PARALLEL GROUPS OF DIASTOLIC PRESSURE

Diastolic B.P. (mm.Hg)	Aware of hypertension		Unaware of hypertension	
	Headache	No headache	Headache	No headache
120	■■□■ □■	+++	□□□ □□	+++++++ +++++++ +++++++ +++++++
125	■■■■ ■■■	++++	□□□	++++++ ++++++
130	■■□■■ ■■□■	+++	□■	+++++++ +++++++
135	■□■ ■□	+	□	++++ ++++
140	■□■■■■■□ ■■■■■■■	++++	□□	++++ ++++
145	■■□■	+		++
150	□■■□■■	++++	□□	++
155	□□■■□	+	■	+
160	■■■■■□	+++		+
165	■	+		++
170	■■■■□.		■	++
175	■			
180				+
185				++
190				
195				
200	■			
Total	71 (74%)	25 (26%)	17 (16%)	87 (84%)

■ Headache volunteered. □ Headache elicited. + No headache.

KNOWLEDGE OF HYPERTENSION

Of the 88 patients with headache 71 (81%) were aware of their raised blood-pressure, whereas of the 112 patients who had no headache only 25 (22%) realised that their blood-pressure was in question; many of them had been sent to the outpatient department because of some complaint unconnected with the cardiovascular system. Since there was no great difference in the average severity of disease between those with headache and those without it, this definite tendency of headache to appear more often among those aware of their condition might be taken to suggest that such knowledge had predisposed

TABLE III—ANALYSIS OF SYMPTOMS OF 25 PATIENTS WITHOUT HEADACHE THOUGH AWARE OF HYPERTENSION

Organic symptoms with hypertensive association	No. of cases	Organic symptoms of unassociated disease	No. of cases	Symptoms coupled with "blood-pressure" and suggesting anxiety	No. of cases	No symptoms	No. of cases
Anginal pain	5	Symptoms associated with carcinoma ..	4	"Dizziness," &c.	1	No symptoms	1
Cardiac asthma ..	1	Melæna (peptic ulcer) ..	1	"Nerves," &c.	1		
Visual difficulties ..	3			"Weakness," &c.	1		
Effort dyspnœa ..	3			"Fainting attacks," &c.	1		
"Fits" (hypertensive encephalopathy) ..	1			"Stuffed-up feelings," &c.	1		
				"Heart bulging out," &c.	1		
Total ..	13		5		6		1

to headache. Cause and effect could not be directly demonstrated, but there appeared a correspondence which might be significant. Such a suggestion must be modified by the admission that a few patients in the survey maintained that they had learnt of their hypertension only after visiting their family doctor because of headache. It was, of course, impossible to judge such a story with accuracy. On close questioning, however, it seemed unlikely that more than a very few of these people had, in fact, originally sought advice because of unexplained headache.

Investigation from the opposite standpoint precluded exposure to this type of error (table II). There were 96 patients who were aware of their hypertension. Of these, 71 (74%) complained of headache. Yet of the 104 patients who did not know of their raised blood-pressure only 3 (less than 3%) volunteered that they had headache. The symptom was elicited from a further 14 (bringing the total to 16%), of whom 12 were women, about half of them of menopausal age. The remaining 87 (84%) denied headache. These 87 were all, nevertheless, severely hypertensive. Their average diastolic pressure was 135 mm. Hg—only a millimetre less than the mean for the whole series. Electrocardiograms suggesting left ventricular "strain" were found in 77% of them, and in 56% radioscopy revealed left ventricular enlargement. Again the retinal damage was relatively less, being of grade II or more severity in only 27%.

The relation between headache and knowledge of hypertension within parallel groups of diastolic pressure is demonstrated in table II. The tendency of headache to appear in conjunction with knowledge of hypertension persists uniformly through the whole range. By contrast, among patients unaware of their hypertension the paucity of headache is striking. In this group the numbers tail off symmetrically upwards through the pressure gradient. This accords with the casual pick-up of an abnormality occurring on a correspondingly diminishing scale of frequency. On the other hand, most of the patients aware of their hypertension were regular attendants at a cardiological outpatient clinic; they thus formed a selected hypertensive sample of the population.

Patients without Headache though Aware of Hypertension

The 25 out of 96 patients who escaped headache, though aware of their hypertension, did not do so because of any relative sparing of their cardiovascular systems. Analysed separately the average diastolic pressure of these patients was 140 mm. Hg; retinal changes of grade II or more were found in 52%, electrocardiographic changes of left ventricular strain in 89%, and radioscopic left ventricular enlargement in 92%—findings which indicate a severity well above the average for the whole series.

All the same these patients, though aware of their hypertension, did not complain of headache. At first sight this fact might be taken as evidence against any view that the symptom, when found among hypertensives, is commonly psychogenic.

To investigate this point the case-histories of these 25 patients were examined in detail. They fell into four groups (table III):

(1) Patients whose attention was centred on some disorder which could be recognised as associated organically with the hypertension—e.g., anginal pain, or visual difficulties for which good cause could be found in the fundi.

(2) The victims of severe incidental disease, usually malignant. The people in these two groups did not attach any importance to their blood-pressure; they had something else to worry about.

(3) Mostly women whose symptoms, and the manner of their expression, suggested anxiety. They complained of "weakness," or "blackouts," or "dizziness" which was neither rotatory nor related to posture. They referred repeatedly to their "blood-pressure." The impression was gained that these patients, knowing their blood-pressure to be raised, found themselves afflicted by symptoms which they subconsciously felt to be appropriate to that disorder. While others might seize upon "headache" they, quite unwittingly, chose something else.

(4) One stalwart avowed that he felt perfectly fit.

Thus, of 96 hypertensives aware of their condition 71 complained of headache, 18 complained, with abundant organic justification, of something else, 6 produced symptoms which bore all the hallmarks of anxiety, and only 1 pronounced himself fit.

Patients with Headache but Unaware of Hypertension

It seemed that a characteristic "hypertensive headache," if indeed such a thing should exist, might certainly be expected to show itself among the patients who complained of headache, without other evident cause, while unaware of their hypertension. It has been pointed out that only 17 of 104 came into this category, a mere 3 complaining of headache spontaneously. The severity of the hypertension affecting these 17, estimated by the usual criteria, was comparatively slight, with an average diastolic pressure of only 131 mm. Hg, this being well below the average for the series. Retinal changes of grade II were found in only 3, while less than half showed minor electrocardiographic and radioscopic abnormalities.

The ages showed a wide scatter. Nevertheless all members of the group were suffering much the same sort of headache. Three-quarters of them had first noticed it within the previous three years, about half of them within eighteen months. Most of them declared that the trouble had been bad but was now getting better. They did not make a great deal of it. Only 1 gave a history of previous migraine. The pain was usually referred to one part of the head—front, back, or either side. It might simulate migraine both in this localisation and in its liability to be precipitated by worry, activity, or excitement. But there was never an aura. The sensation might be described as "thumping," "bumping," or "bursting," the periodicity thus suggested being sometimes related to the pulse-rate. Transient faintness might accompany it. Several patients confined their description to "just an ache." It was often at its worst in the early

morning; this, however, was by no means constant or predictable. When it was severe, nothing short of complete rest and analgesics would relieve it.

MALIGNANT HYPERTENSION

There were 18 patients who had entered the so-called "malignant" phase, in virtue of the development of papillœdema superimposed upon the primary retinal vascular changes. The average diastolic pressure was 159 mm. Hg. A detailed examination was made of this group. To 6 of them the nature of their illness remained unknown. Of these, only 1 complained of headache. On the other hand, 10 of the remaining 12, all aware of their hypertension, complained of this symptom. It thus seems possible that, even with this degree of hypertension, auto-suggestion may sometimes play a part in the production of headache. Again, about half of those who complained of it maintained that it was becoming less. None of them had previously experienced migraine. The average age at onset of the symptom was 40 in men and 33 in women.

The headache endured by these victims of malignant hypertension proved recognisable as a fairly clear-cut entity. It had never been present for long. Very commonly it was referred to one eye, often to the "back" of an eye, or it might be described in terms such as a "pulling of the eye." In addition there might be episodes of transient impairment of vision in addition to a recent progressive deterioration. Usually it was unilateral. It might affect any part of the head. It was often described as "thumping" or "bursting," but again it was evident that these sensations did not always bear a relation to the pulse-rate. Sometimes the pain, for so long as it was present, was "continual." It seldom lasted for more than a few hours at a time. Perhaps its most constant feature was its association with nausea, if not with vomiting. It was evident that to these patients the headache was only a part, and it might be a relatively trivial part, of their affliction. Rarely did it dominate and absorb them, as so often happens with the headache of a space-occupying intracranial lesion. Even without the complications of congestive failure, pulmonary œdema, or uræmia, these unfortunate people felt wretched in a way which they found difficult to define. "I just feel thoroughly miserable" was an expression several times heard. Two of the patients in this "malignant" group might have been said to be experiencing "hypertensive encephalopathy" in that spasmodic headache was accompanied on occasion by transient palsies or by fading of consciousness.

FACTOR OF ANXIETY

It has been pointed out that 104 of the patients in this survey did not know that their blood-pressure was abnormal. Of these, 87 would admit no headache. On the other hand, all but one of those who had learnt of their condition offered symptoms of some kind, those with headache numbering 71 out of 96. These headaches, however, were seldom described in terms bearing any resemblance to those used, with a readily appreciable uniformity, by the few patients who protested headache while ignorant of their disease. Obviously the fact that a patient may have discovered that he has hypertension gives him no exemption from any organic symptom which that disorder may induce. Yet, in fact, most of these 71 patients gave the clear impression that their symptoms stemmed from anxiety consequent on that knowledge.

Those so affected included many elderly women. The ubiquitous "blackout" figured prominently in their stories. "Dizziness" was mentioned specifically by 23 of them; only 5 made this complaint while ignorant of their hypertension. Of the whole 200 no more than 4 or 5 had experienced true vertigo without evident cause in a labyrinth or elsewhere. It then seemed that such vertigo might have an organic origin in the cerebral cortex, analogous to that occasionally presenting in migraine. Usually, however, the complaint of dizziness did not suggest an organic basis.

The headaches of these 71 patients, it was at once evident, had nearly all begun soon after the victims had first learnt of their hypertension. The reality of the complaint was seldom in doubt; but it was described in terms characteristic of anxiety. Commonly it was said to be "continual," in the sense of never ceasing for a moment. Activity, nevertheless, or inert tablets might relieve it. Sometimes it was "bad in the morning." Above all it was evident that "headache" and "blood-pressure" were regarded as a virtually inseparable combination. One lady expressed it: "But I thought blood-pressure *was* headache." A second remarked, perhaps more significantly than she realised: "Before I knew I had this blood-pressure I didn't have any headaches." To all of them it seemed natural and indeed inevitable that, if their blood-pressure was raised, they must have headaches. Many of the people in this survey used the terms "blood-pressure" and "headache" as if they were interchangeable.

CONTROLS

Patients who had complained of headache without any evidence of organic illness were questioned. A neurologist (Dr. A. M. G. Campbell) had judged the background to be one of anxiety. These people often volunteered that their headaches were worse in the early morning. Such timing is, of course, also characteristic both of migraine and of space-occupying intracranial lesions. Moreover, transient indisposition of many kinds can produce, in otherwise normal people, a "hangover" type of morning headache. Such a sensation may, perhaps, become exaggerated, as part of a neurosis, and be experienced daily. Many of these controls complained also of "dizzy feelings." Their symptoms were, in fact, indistinguishable from those offered by most of those hypertensives who had headache while aware of their high blood-pressure.

A further 3 controls had complained incidentally of long-standing headache, for which no reason could be found, after admission to hospital for abdominal surgery. It was suggested to them that the surgical treatment would in all probability achieve the happy additional effect of curing this headache. Six months later all 3 declared their headaches to be much less severe.

Discussion and Conclusions

This survey seems to show that headache can result directly from hypertension. Such headache is rare, but it bears the stamp of an organic symptom. In character it closely resembles migraine. Reasonably, perhaps, it may be supposed that its origin is similar—that it is due, in fact, to intermittent stretch of the cerebral arterial walls, and is analogous to that produced experimentally with histamine by Pickering (1933), Graham and Wolff (1938), and others. Such is the view of Symonds (1946), who holds that a few of the headaches that accompany arterial hypertension appear to have "much the same basis as those of migraine."

On the other hand, it seems to be indisputable that in association with hypertension a second type of headache occurs very often. This headache derives from anxiety. Platt (1950) has said that "very many hypertensive subjects . . . have been given an anxiety neurosis by the discovery of their high blood-pressure. It would not be far from the truth to say that the majority of symptoms of hypertension are iatrogenic." The conclusion to be drawn from the present investigation reinforces that assertion. Supporting evidence was obtained from several sources. Thus of the 104 patients unaware of their hypertension only 3 volunteered that they had headache, a further 14 admitting it; the tendency for headache to be absent persisted symmetrically

through all grades of diastolic pressure. Yet the symptom was complained of, usually in terms strongly suggesting neurosis, by 71 out of 96 comparable hypertensives who knew the nature of their illness. It had then nearly always appeared shortly after their acquisition of that knowledge. Moreover most of the 25 remaining out of this 96 had excellent organic cause for concentrating their attention on something else. Only 1 declared himself to feel well. On the strength of these findings it seemed virtually impossible for a patient to remain symptom-free after being told of his raised blood-pressure.

How are the organic and anxiety types of headache to be distinguished? Features which have been widely held to indicate typical "hypertensive" headache—e.g., exacerbation in the early morning—seem, after all, to be of little diagnostic value. There are, however, better points of distinction; they are summarised in table IV.

On the whole, the organic type of headache has seldom been present for more than a few months. It declares itself soon after the pressure begins to rise, either for the first time, or after a period of stability following an initial increase. The severity of the hypertension, shown by the diastolic pressure and the state of the left ventricle, plays no direct part in its production. In the late stages, however, there is a tendency for advanced retinal changes to be associated with it. It is likely to resemble migraine in its unilateral localisation and in liability to be precipitated by worry or excitement; but there is no aura. Transient faintness, occasionally true vertigo, may accompany it. It seldom lasts for more than a few hours at a time. While severe it responds only to complete rest or powerful analgesics. After a time it tends to become less. The victim is unlikely to be of more than middle age. He is often unaware that his blood-pressure is in question.

By contrast, the onset of the anxiety type of headache follows closely on the patient's first learning of his "blood-pressure." The sufferer may be beyond middle age, commonly an elderly woman. Bizarre complaints, typical of anxiety, accompany the headache, which tends to be perpetual. Suggestion, however, may bring relief.

TABLE IV—COMPARISON OF FACTORS CHARACTERISTIC OF ORGANIC AND ANXIETY HEADACHE FOUND IN ASSOCIATION WITH HYPERTENSION

Organic	Anxiety
Rare	Common
Seldom found over middle-age; in women often at menopause, sometimes much younger	Any age; common in the elderly, particularly women
Often no knowledge of disease	Always knowledge of "blood-pressure"
Short history of headache	Headache dates from the time of acquiring knowledge of "blood-pressure"
Severity of hypertension tends to be: (1) comparatively slight, or (2) "malignant" (state of left ventricle of no account)	Severity (measured by any standard) of no account
Retina changes often severe in later stages of hypertension	Severe retinal changes relatively uncommon
Headache often "bad in the morning"	Headache often "bad in the morning"
Headache made worse by worry, and activity	Headache made worse by worry, may be lessened by activity
Headache often tending to get less	Little spontaneous relief; inert tablets may be effective
Headache like migraine, but no aura; vertigo occasionally; faints more common; in "malignant" phase eye pain, nausea, and feeling of wretchedness	Headache bizarre; typical of neurosis; accompanied by, or alternating with, "black-outs," "dizzy turns," &c.; faints rare; no nausea; no vertigo

Headache of the type which can be supposed organic was found in three main groups of hypertensives:

(1) *Menopausal women.*—Two-thirds of the women volunteering that they had headache were of menopausal age. The symptom may be caused at this period of life by associated organic changes, which are probably vascular.

(2) *With early benign hypertension.*—The average severity of hypertension among the 17 patients who complained of headache while unaware of their hypertension was much below the average for the rest of the series. Moreover three-quarters of these patients had developed their headache comparatively recently, more than half of them declaring that there had already been considerable improvement. Lovibond (1949) has suggested that headache may result, in hypertension, from the first rise in pressure.

(3) *With malignant hypertension.*—Such patients fall into a separate category, which has been described. Deep eye pain, nausea, and severe general malaise are almost constant accompaniments of the headache.

These organic varieties of headache are rare. Should they present in a menopausal woman, or in a patient whose blood-pressure has lately begun to rise, they can confidently be expected to vanish spontaneously, particularly on rest, within an hour or two, and to exhibit a general tendency, over a longer period, to disappear of their own accord. It follows that successful treatment of organic headache caused by benign hypertension can never be identified with certainty. In fact, whatever may be the evidence of success in combating this form of hypertension, the alleviation of headache can never, logically, be part of it.

Nearly all the headaches presenting during the course of benign hypertension are due to anxiety. They are thus likely to respond favourably to any form of treatment that promises benefit. It has been shown by Friedman et al. (1949) that the degree of the response is likely to vary directly with the impressiveness of the treatment adopted. Sympathectomy seems to be well qualified in this respect.

With malignant hypertension the problem is different. In this condition organic headache presents fairly often, even if submerged among other symptoms. Sympathectomy seems to be effective in reducing it. It may be noted, however, that according to Wood (1950b) a mere 0·2% of persons with simple hypertension pass into the malignant phase.

Today there is some hope of cutting short the sinister, and still unexplained, rise in blood-pressure that occurs in hypertension. In particular the new hypotensive drugs show promise. Already it seems that, on occasion, cardiac failure may be postponed, visual difficulty improved, and life prolonged. The future is hopeful. Yet it would be a pity if a confusion of premises should lead to false optimism. Certainly it would be well to remain unimpressed with any measure that bases its claims upon the relief of headache.

Summary

A survey was made of 200 consecutive patients with severe hypertension. The average diastolic pressure, measured under standard conditions of rest, was 136 mm. Hg.

Assessment was made of the symptom of headache, whether spontaneous or elicited by an interrogation technique designed to avoid suggestion.

Those patients who were aware and those unaware of their hypertension were compared. The severity of disease was found to be roughly the same in the two groups, estimated by diastolic level, electrocardiograms, and radioscopic appearances of the left ventricle. Retinal changes were somewhat greater in those with headache.

Of the 104 patients unaware of their hypertension 87 would not admit to having headache. This tendency for headache to be absent persisted symmetrically through all grades of diastolic pressure. The symptom was volunteered by only 3 of these patients, being elicited from the remaining 14. Of 96 patients

aware of their hypertension 71 complained of headache, most of them in terms characteristic of anxiety. On analysis of the remaining 25 it was found that 18 had good organic cause for complaining of something else, and 6 offered symptoms characteristic of anxiety.

From these and other findings, together with evidence afforded by the examination of controls, it was concluded that the headache which so often accompanies hypertension is usually a product of anxiety. Moreover it seems almost impossible for a patient who has been told of his " blood-pressure " to remain symptom-free.

It appeared further that hypertension might occasionally produce headache as an organic symptom. It was most likely to do so in menopausal women, during the early stages of benign hypertension, or, as a relatively insignificant feature, within the syndrome of malignant hypertension.

Analysis was made of factors which serve to distinguish this rare organic headache from the common one which is due to anxiety.

Attention is drawn to the fallacy of acclaiming any treatment of hypertension in virtue of its alleged cure of headache.

This survey was made at the instigation, and with the advice, of Dr. D. H. Davies. Most of the patients concerned were under his care. A few, however, were under the care of other members of the consultant staff of the Bristol Royal Infirmary, to whom, therefore, I should like to express my thanks.

REFERENCES

Alexander, W. A. (1948) *Edinb. med. J.* **55**, 168.
Allen, E. V. (1952) *Circulation*, **6**, 131.
Atkins, H. (1950) See *Brit. med. J.* ii, 344.
Brain, W. R. (1952) Diseases of the Nervous System. London; p. 292.
Chris, S. M. (1951) *Brit. med. J.* i, 665.
FitzGerald, P. (1950) *Lancet*, i, 924.
Friedman, A. P., Brenner, C., Carter, S. (1949) *J. Amer. med. Ass.* **139**, 195.
Graham, J. R., Wolff, H. G. (1938) *Arch. Neurol. Psychiat., Chicago*, **39**, 737.
Hammarström, S., Bechgaard, P. (1950) *Amer. J. Med.* **8**, 53.
Keith, N. M., Wagener, H. P., Barker, N. W. (1939) *Amer. J. med. Sci.* **197**, 332.
Lovibond, J. L. (1949) *Brit. med. J.* i, 833.
Mackey, W. A., Shaw, G. B. (1951) *Ibid*, ii, 259.
Medical Research Council (1950) *Lancet*, ii, 509.
Murphy, E. A. (1951) *Ibid*, ii, 899.
Pickering, G. W. (1933) *Clin. Sci.* **1**, 77.
— (1942) *J. Mt Sinai Hosp.* **8**, 916.
Platt, R. (1950) *Brit. med. J.* i, 951.
Smirk, F. H. (1952) *Lancet*, ii, 695.
— Alstad, K. S. (1951) *Brit. med. J.* i, 1217.
Smithwick, R. H. (1940) *Surgery*, **7**, 1.
— (1948) *Amer. J. Med.* **4**, 744.
Symonds, C. P. (1946) *Guy's Hosp. Gaz.* **60**, 202.
Wood, P. (1950a) Diseases of the Heart and Circulation. London; p. 422.
— (1950b) *Ibid*, p. 436.

INTRA-ARTERIAL TRANSFUSION

THE POTASSIUM HAZARD

D. G. MELROSE, B.M. Oxfd
ASSISTANT LECTURER

A. O. WILSON, B.Sc., M.B. Edin.
REGISTRAR

DEPARTMENT OF SURGERY, POSTGRADUATE MEDICAL SCHOOL OF LONDON

THE replacement of blood with the least possible delay is now regarded as fundamental in the prevention and treatment of shock. Blood may be replaced rapidly either by the intravenous or the intra-arterial route. The pros and cons of intra-arterial transfusion have been discussed by Seeley and Nelson (1952) in a review of most of the pertinent literature, and it may be said that such transfusions can be a life-saving measure and are often the method of choice. The extreme case of resuscitation of the clinically dead has been reported by Negovsky (1945), and Gold et al. (1949) have reported dramatic results in patients with complete circulatory collapse.

The mode of action of such transfusions seems to be that the intra-aortic pressure is rapidly raised to a level sufficient to revoke the intense vasoconstriction previously initiated by the pressoreceptors in the aortic arch and carotid sinus, and hence to promote restoration of normal vascular tone, which in turn permits normal perfusion of the capillary networks, particularly those of the heart and brain, which may even be perfused directly by the ingoing infusion.

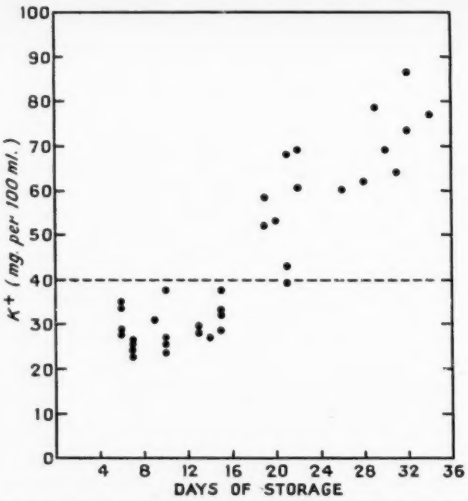


Fig. 1—K+ values of samples from plasma-cell interface of bottled blood.

POTASSIUM IN STORED BLOOD

Intra-arterial transfusions are generally given in emergencies and often in large amounts, and therefore stored blood must usually, if not always, be used. This raises the possibility of adverse effects due to the altered chemical composition of stored blood. Crafoord (1948) expressed a preference for fresh blood when large amounts are to be given rapidly, but did not refer to the question of the chemical composition of the blood.

Mainwaring et al. (1940) and De Gowin et al. (1940) have drawn attention to the rapid release of potassium from the red cells during the storage of blood, and we have confirmed their results (fig. 1). Potassium was determined by means of an internal standard flame photometer based on that described by Berry et al. (1946). Our figures tend to be lower, possibly because of improved methods of storage and because our samples were collected from the region of the plasma-cell interface. Nevertheless plasma-potassium levels of 35 mg. or more per 100 ml. are not uncommon in blood stored for up to three weeks. This figure of 35 mg. of potassium per 100 ml. of plasma is just below the fatal concentration in man, which is about 40 mg. of potassium per 100 ml.

The danger of giving potassium-containing solutions intravenously has been much emphasised (Fenn 1940, Hoffman 1950), and for administration by this route at a rate not exceeding 2 or 3 ml. per minute a safe potassium concentration is about 200 mg. per 100 ml. (50 m.eq. per litre). This would be diluted to give a rise in plasma-potassium level of only about 0·25 mg. per 100 ml. (0·06 m.eq. per litre) per minute, provided the blood volume was normal and all the potassium remained in the plasma. Wright (1952) states: " The high plasma K^+ concentration of stored blood must be borne in mind, as K^+ in excess has toxic effects on the circulation; these may be avoided if the transfusion is performed at rates not exceeding 40 cc. per minute."

In the same context Blixenkrone-Møller (1949) advises against the use of stored blood if many transfusions are to be given in quick succession, even by the intravenous

route. Trumper (1951) has made similar observations on the use of plasma obtained from stored blood in the treatment of burns, and our measurements of the potassium level in twelve samples of plasma withdrawn from 1000-donor pools (fig. 2) confirms that values above 40 mg. per 100 ml. are common. Trumper also drew attention to the fact that, in shock, oliguria and a decreased cardiac output obviously potentiate the effect of any increase in plasma-potassium level, and these same factors operate in the similar but smaller changes in cardiac output and renal function occurring in all surgical patients.

The danger to the patient is largely the effect on the cardiac musculature of too high a concentration of potassium. It *may* be that another determining factor operates—i.e., the rate at which the cells can take up the excess of circulating potassium. Nevertheless a raised plasma-potassium level produces extrasystoles and ultimately death from cardiac arrest in diastole (Best and Taylor 1950).

REDUCTION OF POTASSIUM LEVEL

Since stored blood may contain a high level of potassium, attempts were made to reduce this by various means, so as to make the blood safer for rapid and massive intra-arterial transfusion. Maizels (1949) reinvestigated Harris's (1941) observation that incubation of stored blood at 37°C for a few hours in the presence of glucose causes cation distribution to return to normal. He found, however, that potassium did not return to the cells until after eight hours, the pH and other factors being of great importance in determining the rate. Thus the ideal method of restoring the composition of the blood is unfortunately impracticable.

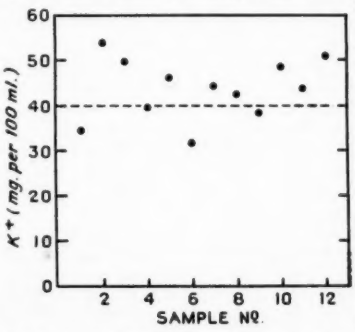


Fig. 2—K+ values of twelve samples of plasma from 1000-donor plasma pool.

Much of the potassium which has diffused out of the red cells may be removed by decanting the plasma from stored blood and reconstituting with physiological saline solution or better, with salt-free dextran, since this would obviate the risks attached to the administration of large amounts of sodium chloride to patients many of whom would be suffering from cardiac disease. It may be argued that this is inadequate since the plasma-potassium level round the sedimented red cells is higher than in the supernatant fluid. The volume of plasma remaining between the cells is, however, relatively small. This method proved to be a useful means of reducing the potassium level, a reduction of over 40% being obtained after replacement of the supernatant plasma by saline solution. Fig. 3 shows the reduction of potassium level in 13 samples of bank blood stored for more than twenty-one days. The cells and saline solution had been gently mixed and the potassium level determined on the "plasma" after centrifuging.

CARDIAC EFFECTS OF EXCESSIVE POTASSIUM

Attempts were also made to demonstrate in the dog the danger of intra-arterial transfusions of blood containing high levels of potassium by studying the effects of these on the electrocardiogram. Though slight changes were noted, no unequivocal evidence was obtained. Nevertheless these changes were probably significant in view of the fact that the fatal potassium level is higher in the dog than in man, and the total amount of potassium given was less than a quarter of that required by Winkler et al. (1938) to produce changes in the electrocardiogram after slow intravenous infusion.

Three important considerations govern the effect of potassium solutions, given intra-arterially on the heart.

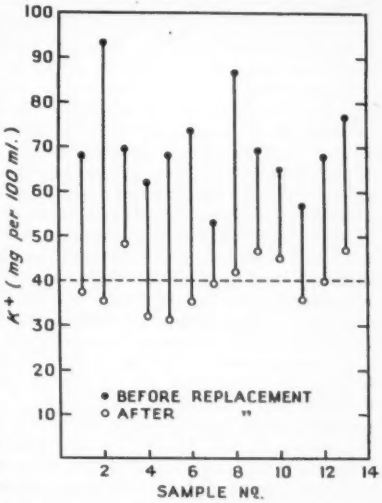


Fig. 3—K+ values of thirteen samples before and after replacement of plasma by isotonic saline solution.

These are the direction of flow of the transfusion, the extent to which it is diluted in its passage to the heart, and the immediate state of potassium metabolism in the recipient. According to the site of infusion and the existing cardiac output, the bulk of the entering blood will go either with the normal stream away from the heart or in a retrograde direction into the coronary vessels. Where the output of the heart is very low a large proportion of the entering blood must go into the coronary vessels, regardless of the site of infusion, and in the stopped heart this undoubtedly happens (Smirenskaia and Maksimishina 1951). Jones et al. (1950) showed that 35% 'Diodrast' injected into the femoral artery of the dog passes directly into the coronary vessels if the systolic blood-pressure is less than 50 mm. Hg. It has further been demonstrated that, even in the presence of a normal cardiac output, the infused fluid may enter the coronary vessels if given into the aorta (Steiner 1952, Page 1946).

If mixing is instantaneous and complete, it is theoretically possible to give with safety a transfusion of 500 ml. of blood a minute, with a plasma-potassium level of as much as 100 mg. per 100 ml. (25·6 m.eq. per litre); for, even if the cardiac output is as low as 2 litres a minute, the level of potassium in the mixed blood reaching the heart should not exceed 36 mg. per 100 ml.—a safe level. In practice it is unlikely that mixing is complete and instantaneous, and the possibility exists that dangerous amounts of potassium may be forced into the heart although the output is not seriously reduced. In those instances where the output is less than 2 litres a minute, and it is under just such conditions that intra-arterial transfusions are particularly indicated, dilution may not reduce to a safe level the amount of potassium in the plasma of stored blood when this is given at an adequate rate. Especially is this likely in operations on the heart, where the output may temporarily fall to nil, and it must be assumed, and indeed is hoped, that the infused blood passes directly into the coronary vessels.

RESUSCITATION

In such circumstances it is essential to have available a simple method of resuscitation. Experience with a modified Henri-Jouvelet rotary pump suggests that it is the ideal device for rapid transfusion into either artery or vein. In use the tube connecting the blood reservoir

to the cannula is simply clamped within the pump, the stationary eccentric roller adjusted to act as a tap, and the usual rate of infusion at about 60 drops a minute may be obtained. To increase the rate of delivery the handle driving the roller is turned manually. No other adjustment is required. Flow-rates of about 400 ml. a minute may easily be achieved by using standard transfusion tubing with pump rotation speeds of 60 a minute. This rate has been found to have of itself no undesirable effects in patients (Melrose and Shackman 1951); and, so far as is known, the only other reference to such rates of administration by the intra-arterial route in man is that of Hitchcock et al. (1952). The danger of gas embolism is very remote with this method, and no demonstrable alteration of the blood is brought about during one passage through the pump.

In intra-arterial transfusions it is inadvisable to inject in any quantity anything but blood. Particularly must dextrose solutions be avoided. A small area of skin adjacent to the site of cannulation into the radial artery is often perfused directly during transfusion into this artery. If saline solutions or dextrose is used, the area becomes totally anoxic and may slough; when blood alone is used, this disturbing side-effect is avoided. There is in fact little justification for giving fluids other than blood by the intra-arterial route, since they possess no oxygen-carrying power and the stay of glucose and saline solution within the circulation is evanescent.

At present there is insufficient experience of intra-arterial transfusions to solve all the problems involved. The best rate of administration is not yet known, although it seems probable that the higher rates of about 300 ml. a minute are better. If blood-transfusion is required at lower rates than this, it is generally possible to give it by the intravenous route rather than by the more complicated intra-arterial infusion. The general trend seems to be towards unnecessarily complex machines, even though a simple pump system is adequate.

Fortunately it is becoming appreciated that blood is the only fluid suitable for administration by the intra-arterial route, but we still have insufficient knowledge of the immediate fate of the blood in the circulation, and the advantages and disadvantages of this method of therapy have yet to be assessed.

SUMMARY

Intra-arterial transfusion may be needed to save life.

Blood alone should be used.

If stored blood is used, precautions should be taken that the plasma-potassium level is not dangerously high.

The plasma-potassium level of stored blood increases with length of storage and may exceed 40 mg. per 100 ml. (10 m.eq. per litre)—a concentration which is lethal to man.

Simple decanting of plasma and reconstituting with saline solution or with dextran will lower the plasma-potassium to safer levels.

Rapid transfusions, both intravenous and intra-arterial, are safely and easily given with a simple rotary pump.

We are indebted to Miss M. McKay, Blood Group Reference Laboratory, Chelsea, London, for the samples of pooled plasma.

REFERENCES

Berry, J. W., Chappell, D. G., Barnes, R. B. (1946) *Industr. Engng Chem.* (Anal. Ed.) **18**, 19.

Best, C. H., Taylor, N. B. (1950) The Physiological Basis of Medical Practice. London.

Blixenkrone-Møller, N. (1949) *Acta chir. scand.* **97**, 300.

Crafoord, C. (1948) *Ann. Surg.* **128**, 879.

De Gowin, E. L., Harris, J. E., Plass, E. D. (1940) *J. Amer. med. Ass.* **114**, 855.

Fenn, W. O. (1940) *Physiol. Rev.* **20**, 377.

Gold, I. B., Rosenthal, J. L., Schotz, S. (1949) *Curr. Res. Anesth.* **28**, 319.

Harris, J. E. (1941) *J. biol. Chem.* **141**, 579.

References continued at foot of next column

POLIOMYELITIS FOLLOWING INOCULATION

A SURVEY OF 29 CHILDREN

DENNIS GEFFEN
M.D. Lond., D.P.H.
MEDICAL OFFICER OF HEALTH, METROPOLITAN BOROUGHS OF ST. PANCRAS AND HAMPSTEAD

J. HAMILTON PATERSON
M.D. Lond., M.R.C.P.
PHYSICIAN TO THE NEUROLOGICAL DEPARTMENT, ST. GEORGE'S HOSPITAL; ASSISTANT PHYSICIAN TO THE NATIONAL HOSPITAL FOR NERVOUS DISEASES, QUEEN SQUARE, LONDON

S. M. TRACY
M.R.C.S., D.P.H.
DEPUTY MEDICAL OFFICER OF HEALTH, METROPOLITAN BOROUGH OF ST. PANCRAS

DURING September, 1949, one of us (D. G.) became aware of an association between immunisation against diphtheria and/or whooping-cough and the incidence of paralytic poliomyelitis; accordingly a preliminary report on the subject was sent to the Chief Medical Officer, Ministry of Health, and the Medical Officer of Health for the County of London.

This association between poliomyelitis and inoculation appeared to apply chiefly to the use of a diphtheria-pertussis combined prophylactic; as a result its use in London was discontinued in the following month.

The matter was submitted to Prof. A. Bradford Hill and Dr. J. Knowelden, who concluded that, in the 1949 epidemic of poliomyelitis in this country, cases of paralysis were occurring which were associated with inoculation carried out within the month preceding the recorded date of onset of the illness (Hill and Knowelden 1950). At about the time this matter was made public (Geffen 1950) other reports confirmed these findings, both in this country (Martin 1950) and in Australia (McCloskey 1950).

In 1949 it seemed that this association between inoculation and poliomyelitis was possibly confined to Britain and Australia, for, in correspondence with American authorities, one of us (D. G.) was informed that similar occurrences had not been noted in U.S.A., where both the rate of immunisation and the incidence of poliomyelitis are very high. However, in 1951 Anderson and Skaar, of Minneapolis, published a paper on poliomyelitis occurring after injections of antigen. Their report was based on data collected in 1946. They came to the following conclusions:

(1) In poliomyelitis patients who had received some antigen in the previous month there was a high degree of correlation between the site of paralysis and the site of injection.

(2) Such cases tended to show a different distribution of paralysis, with more severe involvement, than did comparable children immunised from two to six months previously, in previous years, or not at all.

DR. MELROSE, DR. WILSON: REFERENCES—*continued*

Hitchcock, C. R., Smith, L., Varco, R. L. (1952) *Surgery*, **32**, 58.

Hoffman, W. S. (1950) *J. Amer. med. Ass.* **144**, 1157.

Jones, P. G., Davis, J. H. jun., Hubay, C. A., Holden, W. D. (1950) *Surgery*, **27**, 189.

Mainwaring, B. R. S., Aylward, F. X., Wilkinson, J. F. (1940) *Lancet*, ii, 385.

Maizels, M. (1949) *J. Physiol.* **108**, 247.

Melrose, D. G., Shackman, R. (1951) *Lancet*, i, 1144.

Negovsky, V. A. (1945) *J. Amer. med. Ass.* **129**, 1226.

Page, I. H. (1946) *Cleveland Clin. Quart.* **13**, 1.

Seeley, S. F., Nelson, R. M. (1952) *Int. Abstr. Surg.* **94**, 209.

Smirenskaia, E. M., Maksimishina, U. V. (1951) *Surgery, Moscow*, no. 5, p. 14; *Abstr. World Surg.* **10**, 227.

Steiner, R. E. (1952) Personal communication.

Trumper, M. (1951) *Surg. Clin. N. Amer.* p. 1551.

Winkler, A. W., Hoff, H. E., Smith, P. K. (1938) *Amer. J. Physiol.* **124**, 478.

Wright, S. (1952) Applied Physiology. London.

(3) The interval between injection and the subsequent onset of poliomyelitis suggested some relationship other than chance.

More recently Korns et al. (1952) have studied the association between poliomyelitis and parenteral injections of all kinds by collecting data from 2137 poliomyelitis patients in 1950, from 6055 members of the patients' households, and from 14,710 other controls living in adjacent houses.

They found that their poliomyelitis cases had had twice as many injections of all kinds in the two months before the onset of poliomyelitis than had the controls of similar age, and they conclude that their data tend to indicate that the risk of poliomyelitis is doubled during the two months following an injection of an immunising substance, penicillin, or other materials. In addition, like the workers previously mentioned, they found a positive correlation between the site of paralysis and the site of injection. They state that, although the cases are few, it may be worth recording that in their study the mean interval between immunising injections in the arm and paralysis was twenty-three days, whereas for injections in the leg it was thirty days. They noted that paralysis tended to be slightly more severe after injections than where there had been no injections.

The main aim of our survey reported here was to assess the amount of subsequent recovery in the children who were the subject of a previous report (Geffen 1950).

McCloskey (1952) has also compared the recovery of 25 children whose poliomyelitis had followed recent inoculation (upon whom he had reported in 1950) and 65 children in whom there was no such history. The inoculated groups contained a higher proportion of cases of severe paralysis; but, when cases of equal initial severity were compared, the residual paralysis after eighteen months was not significantly different in the two groups.

Observations

In the earlier report (Geffen 1950) reference was made to 37 children, of whom 30 had developed poliomyelitis within a month of immunisation, the site of paralysis being the site of injection. None of these subsequently died, and we have seen and examined 27 of these 30 children some two years later. Of the other 3, we have full hospital records of the illness and present condition of 2 (cases 2 and 12), but 1 (case 9) remains untraced, though there is no reason to doubt that he is alive.

In order to get a comparison of the extent of recovery, we also obtained the history and examined another 23 children who had not had any recent injection but who had developed poliomyelitis at about the same time in London in 1949, who were of approximately the same age, and in 21 of whom an upper limb was one of the limbs affected.

In the course of examining these children we came across one child (case 28) who had developed paralytic poliomyelitis affecting the left upper arm, the onset of illness being fourteen days after an injection of partussis vaccine. We have therefore transferred this child to the survey of recovery of children who suffered from post-inoculation paralytic poliomyelitis. We also had referred to us another child (case 29) who received an injection of alum-precipitated toxoid (A.P.T.) on Oct. 5, 1949, in the left arm and developed paralytic poliomyelitis affecting the left upper arm on Oct. 15, 1949, and we have included this child as well.

We have omitted 2 of the original cases for the following reasons:

(1) In one case the interval between injection and paralysis was about a month; but, though the child was injected in

TABLE I—INOCULATED CASES

Case no.	Sex	Age at onset of illness	Reagent	Limb of injection	Interval between injection and onset of poliomyelitis (days)	Maximum paralysis	Present state
1	F	9 mths	*Combined	L. arm	14	L. arm severe R. leg slight	L. arm slight R. leg nil
2	M	10 mths	Combined	L. arm	12	L. arm very severe L. leg ,, ,, R. leg moderate	L. arm very severe L. leg ,, ,, R. leg nil
3	F	11 mths	Combined	L. arm	21	L. arm very severe	L. arm severe
4	M	1 yr 5 mths	Combined	L. arm	12	L. arm severe	L. arm slight
5	F	9 mths	Combined	L. arm	12	L. arm very severe R. arm ,, ,, R. leg moderate L. leg slight	L. arm very severe R. arm severe R. leg moderate L. leg slight
6	F	2 yrs 10 mths	Combined	R. arm	16	R. arm very severe	R. arm severe
7	M	1 yr 3 mths	Combined	L. arm	10	L. arm very severe	L. arm severe
8	F	10 mths	Combined	L. arm	12	L. arm very severe	L. arm moderate
9	M	1 yr 11 mths	Combined	L. arm	15	L. arm very severe	L. arm severe
10	M	10 mths	Combined	L. arm	26	L. arm very severe R. arm ,, ,, R. leg severe	L. arm very severe R. arm ,, ,, R. leg severe
11	M	10 mths	Combined	R. arm	8	R. arm very severe L. leg moderate	R. arm severe L. leg slight
12	F	10 mths	Combined	R. and L. thighs	15	L. leg very severe R. leg severe	L. leg severe R. leg slight
13	M	11 mths	Combined	L. thigh	22	L. leg very severe	L. leg severe
14	M	2 yrs 3 mths	†A.P.T.	L. arm	9	L. arm very severe R. leg moderate	L. arm very severe R. leg slight
15	F	1 yr 7 mths	A.P.T.	L. arm	7	L. arm moderate	L. arm slight
16	M	1 yr 1 mth	A.P.T.	L. arm	24	L. arm very severe	L. arm moderate
17	F	1 yr 2 mths	A.P.T.	L. arm	11	L. arm very severe	L. arm severe
18	M	9 mths	Combined	L. arm	5	L. arm very severe	L. arm severe
19	M	1 yr 1 mth	Combined	L. arm	16	All 4 limbs very severe	All 4 limbs severe
20	M	1 yr	Combined	L. arm	12	All 4 limbs very severe	L. arm very severe R. arm severe R. leg slight L. leg nil
21	F	1 yr	Combined	L. arm	8	L. arm very severe	L. arm moderate
22	F	4 yrs 6 mths	A.P.T.	L. arm	11	L. arm very severe	L. arm severe
23	F	11 mths	A.P.T.	L. arm	9	L. arm very severe	L. arm very severe
24	M	1 yr 3 mths	A.P.T.	L. arm	8	L. arm very severe	L. arm moderate
25	F	10 mths	A.P.V.	L. arm	8	L. arm very severe	L. arm moderate
26	M	1 yr	Combined	L. arm	36	L. arm severe	L. arm moderate
27	F	1 yr 11 mths	Combined	L. arm	9	L. arm very severe	L. arm severe
28	M	4 yrs 11 mths	‡A.P.V.	L. arm	16	L. arm severe	L. arm moderate
29	M	10 mths	A.P.T.	L. arm	10	L. arm very severe	L. arm very severe

* Combined diphtheria—pertussis prophylactic.
† A.P.T. = alum-precipitated toxoid (diphtheria).
‡ A.P.V. = ,, ,, vaccine (pertussis).

the left arm, it was the right shoulder and left leg which were mainly affected.

(2) In another case the interval was about a month, but there was no definite information about the site of the inoculation.

Originally some doubt was expressed as to whether the paralysis ensuing on inoculation in these and similar children was in fact due to poliomyelitis. As it is now generally accepted that this is so, we shall not discuss the matter in detail; but it is of interest that MacCallum (1950) isolated poliomyelitis virus from the stools of 2 of our children who had been inoculated in the subsequently paralysed limb eleven and twelve days previously. Further, 26 of our 29 inoculated children had a lumbar puncture in the acute stage of their illness, and the cerebrospinal fluid was characteristic of poliomyelitis.

Table I relates to 29 children who developed poliomyelitis in 1949 following recent inoculation, the limb of inoculation becoming subsequently the limb of major paralysis or one of the parts maximally involved. The extent of paralysis at the height of the illness and about two years later (" present state ") was assessed in accordance with the following scale, which is similar to that adopted by McCloskey (1952):

Very Severe.—Flaccid paralysis involving the major part of an extremity.

Severe.—Paralysis of at least one muscle group.

Moderate.—Partial paralysis of at least one muscle group.

Slight.—Slight paralysis involving a muscle group.

Nil.—No detectable weakness.

TABLE II—CONTROLS

Case	Sex	Age at onset of illness	Maximum paralysis	Condition 2 years later
A	M	1 yr 7 mths	L. arm very severe	L. arm severe
B	F	7 mths	L. arm slight L. leg very severe R. leg ,, ,,	L. arm nil L. leg severe R. leg ,,
C	M	2 yrs 6 mths	R. leg very severe	R. leg very severe
D	F	2 yrs	R. arm moderate L. arm slight L. leg moderate	R. arm moderate L. arm nil L. leg slight
E	F	5 mths	L. arm very severe L. leg ,, ,, R. leg ,, ,,	L. arm very severe L. leg ,, ,, R. leg ,, ,,
F	M	8 mths	L. arm moderate R. arm ,, L. leg ,, R. leg very severe	L. arm nil R. arm ,, L. leg ,, R. leg very severe
G	F	1 yr 11 mths	R. arm very severe R. leg moderate	R. arm severe R. leg nil
H	M	3 yrs 6 mths	R. arm severe	R. arm severe
I	M	2 yrs 3 mths	R. arm very severe L. arm ,, ,, R. leg severe L. leg ,,	R. arm very severe L. arm nil R. leg moderate L. leg ,,
J	M	2 yrs 10 mths	L. arm very severe R. arm severe	L. arm very severe R. arm nil
K	F	3 yrs 6 mths	L. arm moderate R. arm slight	L. arm slight R. arm nil
L	M	1 yr 4 mths	L. arm slight L. leg ,, R. leg ,,	L. arm nil L. leg ,, R. leg slight
M	M	1 yr	L. arm very severe	L. arm severe
N	M	1 yr 8 mths	R. leg severe L. leg moderate	R. leg moderate L. leg nil
O	F	1 yr	R. arm severe	R. arm moderate
P	F	1 yr 11 mths	L. arm severe L. leg ,, R. leg moderate	L. arm nil L. leg moderate R. leg slight
Q	F	2 yrs	L. arm very severe	L. arm severe
R	M	2 yrs 9 mths	L. arm severe	L. arm severe
S	M	3 yrs	R. arm severe R. leg moderate	R. arm moderate R. leg nil
T	F	1 yr 6 mths	L. arm very severe L. leg severe	L. arm severe L. leg nil
U	F	3 yrs	R. arm moderate	R. arm nil
V	M	4 mths	L. arm moderate L. leg ,, R. leg ,,	L. arm nil L. leg moderate R. leg nil
W	M	1 yr	L. arm moderate R. arm ,, R. leg ,,	L. arm nil R. arm slight R. leg moderate

TABLE III—AGE AND SEX DISTRIBUTION OF THE INOCULATED AND CONTROL GROUPS

Age at onset (mths)	Inoculated			Controls		
	Males	Females	Total	Males	Females	Total
Less than 12 ..	6	7	13	2	2	4
12–23	8	4	12	5	4	9
24–35	1	1	2	4	2	6
36 or more ..	1	1	2	2	2	4
Total ..	16	13	29	13	10	23

CONTROLS

For purposes of comparison we obtained details of 23 children who had acute poliomyelitis in the same epidemic and in the same city (London) as did our inoculated cases. We have also examined them recently—i.e., from two to two and a half years later. Their particulars are set out in table II. These children were about the same age as the inoculated children, and in 21 of them an upper limb was one of the limbs affected.

Unfortunately we were not able to match the two groups accurately in respect of these factors, but in respect of age all but 27 of the 29 inoculated children and 19 of the 23 controls were aged less than 3 years when they contracted poliomyelitis. The sex-distribution was about the same. Table III summarises the age and sex distribution in the two groups.

INTERVAL BETWEEN INOCULATION AND ONSET OF POLIOMYELITIS

Table I shows that the interval between the last injection and the onset of poliomyelitis was from five to thirty-six days. Here a difficulty arises because in some cases the first day of the disease is reported as the day the first symptoms were noticed—often diarrhœa and vomiting, restlessness, or the like—whereas in other cases the first day of illness obviously refers to the time when paralysis became evident.

We have carefully examined the cases where the incubation periods are twenty-one or more days, and we find the position to be as follows:

Case 3.—Here the interval was twenty-one days between immunisation and onset of poliomyelitis, and there was flaccid paralysis of the left upper arm by the time the child had been admitted to hospital. The onset was said to have been sudden, but there is a history that the child had diarrhœa, passing five or six greenish stools, three or four days previously.

Case 10.—Here the interval was twenty-six days, and the child had been treated at home with sulphonamides for tonsillitis two weeks before the mother noticed that he could not sit up or use his arms.

Case 13.—Here the interval was twenty-two days between injection and the day on which stiffness of the neck and spine, with commencing paralysis, came on.

Case 16.—Here the interval was twenty-four days. There were two notes: a statement, made by the mother two years later, that the child had had an injection a week before he was taken to hospital; and a note in the hospital records to the effect that the child had been immunised two weeks before admission. The official date, however, given us for the last injection by the medical officer of health of the district in which the child was resident, was Aug. 16, 1949, twenty-four days before the onset of poliomyelitis.

Case 26.—Here the interval was thirty-six days, and poliomyelitis was not diagnosed before the boy was taken to hospital by his mother because he was not using his left arm. On admission there was complete flaccid paralysis of this limb. There is no history of illness before this, but possibly there were preparalytic symptoms which escaped recognition.

It is not surprising that in many cases the diagnosis rests on the presence of gross paralysis, because the patients were mostly of an age at which minor illness would not be associated in the mother's mind with the onset of poliomyelitis. Further, it is of course quite

possible for a parent to miss paresis or paralysis when a baby is ill, listless, and apathetic, and has to have everything done for it. The preparalytic symptoms observed in our cases are discussed below.

Fig. 1 is based on the intervals stated in table I, and shows that the average interval was about thirteen and a half days, being twelve days in 5 cases, from five to eleven days in 13 cases, and from fourteen to thirty-six days in 11 cases. In 24 cases (more than 82%) it was from five to sixteen days. We doubt whether some of the longer intervals are correct. The point is important because in a district where poliomyelitis is present, the medical officer of health and the physicians practising there are anxious to know the maximum duration of the period

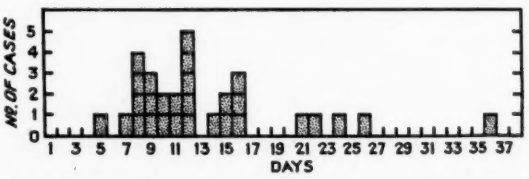


Fig. I—Number of days between injection and onset of symptoms of poliomyelitis.

of risk in this connection. It is also important in differential diagnosis. Hill and Knowelden (1950) say:

"There is no evidence whatever that inoculations carried out in the more distant past have any effect at all upon the incidence or localization of paralysis. These effects appear to be confined to injections given within about a month of the onset of poliomyelitis, and after that interval from inoculation has elapsed no risk need be envisaged."

While agreeing entirely with this statement we think that the period of risk can be further shortened. Taking into consideration the possibility that some mothers have not sought medical advice until such time as illness is acute or paralysis is present, it is probably fair to say that, if a child shows no signs of illness distinguishable by a medical practitioner within two or three weeks of injection, the period of risk has passed.

PREPARALYTIC DISTURBANCES

In table IV the preparalytic symptoms and signs recorded in the inoculated and control groups of children are summarised. These are in almost every instance

TABLE IV—PREPARALYTIC SYMPTOMS AND SIGNS IN 29 CHILDREN WHO DEVELOPED POLIOMYELITIS AFTER INOCULATION AND IN 23 CONTROLS

Symptom or sign	Inoculated group	Controls
Fever	20 (69%)	16 (70%)
Vomiting	17 (58%)	9 (39%)
Drowsiness	16 (56%)	9 (39%)
Injected fauces	13 (45%)	5 (22%)
Anorexia	8 (28%)	3 (13%)
Diarrhœa	6 (21%)	2 (9%)
Headache	3 (11%)	2 (9%)
Coryza	0 (0%)	4 (18%)

such that it would be difficult for a layman to associate them with poliomyelitis. In both the inoculated and control groups the commonest manifestations are fever, vomiting, drowsiness, and injected fauces. Most of our children were too young to complain of headache; those that did were aged 2 years or more.

Clearly the numbers are too small to allow any conclusions to be reached about any significant differences in the preparalytic symptoms in the two groups. In any case it has already been seen that the inoculated children were somewhat younger than the controls, a factor which might well influence their preparalytic signs and symptoms.

TABLE V—PARALYSIS IN INOCULATED LIMBS OF 29 CHILDREN

Initial paralysis and no. of cases	Residual paralysis			
	Very severe	Severe	Moderate	Slight
Very severe 24	8	11	5	..
Severe .. 5	..	..	2	3
Moderate .. 1	..	..	..	1
Slight	..	..	..	..

One child was inoculated in both thighs.

EXTENT OF RECOVERY

Tables I and II reveal the degree of recovery in approximately two years in the inoculated limbs in our 29 patients with post-inoculation poliomyelitis and in the most severely affected limbs in the 23 controls.

Tables V and VI summarise this information for purposes of comparison between the two groups. They show, as one might expect, that the degree of recovery in either group is related to the severity of the original paralysis. In addition, however, they show that, whereas the paralysis in the inoculated limb was nearly always initially severe or very severe, the limb of major paralysis in the controls was not uniformly seriously affected.

The state of all four extremities in both groups is summarised in tables VII and VIII, where the degree of initial involvement is contrasted with the residual state found some two years later. It will be seen that in the series of 29 inoculated children 46 out of 116 limbs

TABLE VI—PARALYSIS IN MAXIMALLY AFFECTED LIMBS OF 23 CONTROL CHILDREN

Initial paralysis and no. of cases	Residual paralysis				
	Very severe	Severe	Moderate	Slight	Nil
Very severe .. 11	6	5	..	..	..
Severe 6	..	2	4	..	..
Moderate .. 5	..	..	1	1	3
Slight 1	..	..	..	1	..

(39·7%) were involved; the comparable figures for the controls being 49 out of 92 (53·3%). This difference tends to confirm our clinical impression that the paralysis of post-inoculation poliomyelitis, though severe, was more limited in extent than in comparable uncomplicated cases. The initial paralysis was severe or very severe in 39 limbs of the injected children, and in 27 cases (69·2%) remained so two years later. A similar state was found in the controls, the comparable figure being 64%. It therefore seems that the difference in recovery in limbs affected to a more or less equal extent in the inoculated and control groups is not of significance.

Discussion

PROPHYLACTIC AGENT

Table I shows that a combined diphtheria-pertussis prophylactic was used in 19, A.P.T. in 8, and pertussis vaccine alone in 2 of our 29 children who subsequently developed paralytic poliomyelitis. Unfortunately we do not know the over-all proportion of children immunised

TABLE VII—STATE OF ALL LIMBS IN 29 INOCULATED CHILDREN

Initial paralysis	No. of extremities	Residual paralysis				
		Very severe	Severe	Moderate	Slight	Nil
Very severe ..	33	9	17	5	1	1
Severe	6	..	1	2	3	..
Moderate ..	5	..	..	1	3	1
Slight	2	..	..	..	1	1
Nil	70	..	..	..	..	70
Total ..	116	9	18	8	8	73

TABLE VIII—STATE OF ALL LIMBS IN 23 CONTROLS

Initial paralysis	No. of extremities	Residual paralysis				
		Very severe	Severe	Moderate	Slight	Nil
Very severe ..	15	7	7	..	..	1
Severe	10	..	2	6	..	2
Moderate ..	17	..	..	3	4	10
Slight	7	..	..	..	1	6
Nil	43	..	..	..	..	43
Total ..	92	7	9	9	5	62

with a combined reagent, compared with A.P.T. and pertussis vaccine in the areas whence these children came in 1949. Such a small series would render invalid any attempt at assessing the relative danger incurred in using any particular type of prophylactic in these circumstances. Yet it is generally agreed that the combined prophylactic was implicated in that year more often than would have been explained by the frequency with which it was used. Perhaps it is significant that, since the use of this vaccine in London clinics was discontinued in October, 1949, very few cases of post-inoculation poliomyelitis have occurred in the London area, although due allowance must be made for the fact that in the subsequent two years far fewer cases of poliomyelitis were notified in the age-groups concerned.

To reduce the local reaction following the inoculation Bousfield (1950) advises subcutaneous instead of intramuscular injection of the reagent. We do not know whether this would have a significant effect on the issue, for we have no information about the depth of the inoculations given in our series or in other children of the same age so protected at that time.

AGE OF INOCULATED CHILD

Bousfield (1950) has also suggested that immunisation during the first few months of life would minimise the risk of post-inoculation poliomyelitis. This may be true to some extent, but it is clear that poliomyelitis may give rise to paralysis in even the youngest infants. Smallpeice and Ounsted (1952) described 3 such cases in infants aged 7, 3, and 2 weeks. Wright and Owen (1952) recorded 3 similar examples of early infantile poliomyelitis. Logan (1952) published figures showing the incidence of poliomyelitis in England and Wales in 1950 for children aged less than 1 year: 254 such children were notified as having paralytic poliomyelitis. Of these, 10% were aged less than 3 months and 18% between 3 and 6 months; hence 72 (28%) of these children had paralytic poliomyelitis before they were 6 months old. It therefore seems unlikely that earlier immunisation would effectively prevent this serious complication.

POST-INOCULATION POLIOMYELITIS AND ANTI-DIPHTHERIA CAMPAIGN

The association between injections and poliomyelitis has naturally received some publicity in the lay press as well as in medical journals, and many medical writers have suggested that this has been unfortunate in that it has given rise to public alarm which has been both unnecessary and out of proportion to the actual situation. It has been argued, for example, that the recent reduction in the number of children immunised against diphtheria is due to this cause, although Gray and Cartwright (1952) have recently concluded that the fear of contracting poliomyelitis after immunisation does not at present constitute a factor of importance in the immunisation campaign. So far as our experience is concerned, we are in agreement with them, having questioned mothers whose children contracted poliomyelitis in 1949 in these circumstances, and who have since had another child.

If the incidence in London of diphtheria and poliomyelitis in recent years (fig. 2) is considered, it is easily seen that the public in this city has every reason to be more worried about poliomyelitis than diphtheria, not only because the case-incidence and death-rate of poliomyelitis are higher but also because the crippled state of some of the survivors of acute poliomyelitis contrasts forcibly with the present rarity of serious diphtheritic sequelæ.

We believe that the public is entitled to know the facts of the situation. These should be put before them fairly and without exaggeration, for in our experience a well-informed public can assess the situation and make a wise decision.

Summary

A report is presented showing the extent of recovery of 29 London children who developed paralytic poliomyelitis in 1949 after a recent inoculation. Comparison is made with 23 children of about the same age who had not had a recent inoculation but had developed paralytic poliomyelitis during the same epidemic, and in 21 of whom an upper limb was affected.

There was no fatality in the 29 inoculated children.

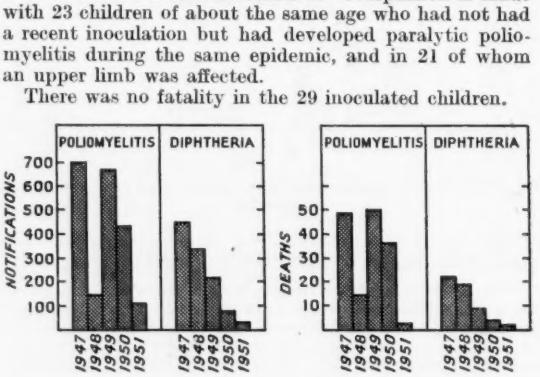


Fig. 2—Comparison between notifications and mortality of poliomyelitis and diphtheria in London.

The average interval between inoculation and the onset of poliomyelitis was thirteen or fourteen days: in over 80% of cases it was between five and sixteen days. It is probable that three weeks after inoculation the period of risk has passed.

The preparalytic symptoms recorded in the 29 inoculated children were in the main similar to those observed in the controls.

The paralysis of poliomyelitis following recent inoculation appears to be relatively limited in extent. When paralysis occurs in an inoculated limb, such paralysis is nearly always severe. Recovery of a limb appears to depend on the initial severity of the paralysis, irrespective of whether the limb has been inoculated or not. The extent of recovery which took place in two and a half years in both the inoculated and control groups was related to the severity of the original paralysis.

In the 29 inoculated children there was no information that the inoculations were intramuscular rather than subcutaneous.

It is considered doubtful if immunisation at an earlier age would prove effective in avoiding post-inoculation poliomyelitis.

It has not been proved that lay publicity on post-inoculation poliomyelitis is the reason for recent reduction in the number of children immunised against diphtheria. We are of opinion that the public is entitled to have the facts put before them clearly.

This work was done with the support and help of a grant from the Medical Research Council.

References at foot of next column

A METHOD OF TREATMENT FOR VARICOSE VEINS

MICHAEL G. WILSON
M.B. Leeds, F.R.C.S.
SENIOR SURGICAL REGISTRAR, BRISTOL ROYAL INFIRMARY

THE method of treatment described here has been used in 50 cases at the Bristol Royal Infirmary with encouraging results.

There is general agreement that when the internal saphenous vein is incompetent and varicose the first step in treatment is its ligation at the point of entrance into the femoral vein. But usually this does not suffice for cure, and many different procedures have been introduced to deal with the residual varicosities in the leg:

Excision of the vein through a long incision (Madelung 1884) is a major procedure which is very occasionally necessary but leaves an unsightly scar. The vein may be removed through small incisions with Mayo's (1906) stripper or Babcock's (1907) acorn-tipped guide. Both these methods tear across tributaries and may cause hæmatomata.

Sclerosants may be injected to obliterate the vein either after operation (Tavel 1904) or at the same time (Schiassi 1908). A ureteric catheter may be used to make the injection (Unger 1927). Disadvantages of the use of sclerosants are the production of thrombosis in the deep veins (Atlas 1943), damage to valves in the deep veins (Kinmonth 1948), and, if the injection is made at the time of operation, a painful leg which tends to discourage early ambulation.

Electrocoagulation as an alternative or an adjuvant to the use of sclerosants by passing a cystodiathermy electrode along the vein was suggested by Smith (1944), but there is difficulty in passing the electrode along tortuous veins and in regulating the current. All these methods of inducing clotting in the veins may be followed by recanalisation.

Multiple ligature of the internal saphenous vein is now the most popular method of dealing with varicosities, and the tendency is to tie the vein in more places. Sclerosants are being reserved to obliterate what varicosities remain after multiple ligature and for minor varicosities of the calf without demonstrable incompetence of the main saphenous trunk.

McElwee and Maisel (1947), following on the work of Moore and Knapp (1942) at the New York Hospital, have compared the results obtained in five different methods used unselectively, and placed them in the following order: (1) multiple ligation; (2) high ligation and retrograde injection; (3) high ligation and stripping; (4) high ligation and excision; and (5) high ligation alone. In all cases postoperative injections were given to complete the obliteration. Although McElwee and Maisel concluded that multiple ligature (with an average of four ligatures) gave the best results in their follow-up (average of eighteen months), they record that an average of 3·4 injections was required later to complete the obliteration, and that minor wound sepsis and delayed healing were troublesome.

The more ligatures, within reason, that are used at the primary operation, the fewer injections are needed later and the better the end-results should be; but as the operation becomes more lengthy and severe, the patient becomes less willing to be ambulant immediately afterwards. Also the incidence of minor wound troubles is higher, and an operation which may have been performed largely to remove unsightly veins may substitute unsightly scars.

A method which can increase the number of permanent interruptions of the veins and at the same time abolish the incisions down the leg would have obvious advantages over those discussed hitherto. Goldstone (1943) suggested, as a substitute for high ligation, the passage of a ligature round the upper part of the saphenous vein by a neat trick in which only two punctures are made, the ligature remaining in situ under the skin. As a substitute for a formal high ligation this is unacceptable; but, if a non-absorbable ligature material, such as braided 'Nylon' is used, it is an effective means of applying multiple ligatures. It is done quickly—a dozen ligatures can be placed in as many minutes—and leaves practically no trace. Consequently a larger number of points can be reasonably ligated, and all the varicosities can usually be completely obliterated at the primary operation. This is the basis of the method described here.

Other percutaneous methods, notably those of Davat (1837) and Schede (1877), have been described; but they are not comparable, because the ligature was tied outside the skin and removed later.

In Davat's method a needle was passed through the skin under the vein and left there while a figure-of-eight ligature was tied tightly round its protruding ends. In Schede's method the ligatures were tied over a rubber tube. In both methods the object was to induce thrombosis and perhaps to cut through the vein. Neither method was very successful; both are crude and have long been obsolete.

Technique

Preliminary Marking

The marking out of the veins before operation is of great importance because it is then that the situation and numbers of ligatures to be used are decided. Hartley's ink * is suitable for this purpose; it produces a deep black mark which does not wash off when the skin is "sterilised" at operation. The incompetent internal saphenous vein is marked off at intervals of 2–4 in. wherever it can be seen or palpated; varicose tributaries are also marked off and at shorter intervals if necessary. Where a large varix is very close to the skin and appears to be adherent to it, ligatures are placed above and below. It is probably better to avoid tying veins immediately over the subcutaneous border of the tibia, especially if the patient is thin.

A suitable method of marking is to place a dot where the punctures will be made, on either side of the vein and about $^3/_4$ in. away from it, so that the two dots are about $1^1/_2$ in. apart with a dash between to link them (fig. 1). If there are large blow-outs that need excision, a line is placed over them.

In some cases it is helpful to have an infra-red photograph of the leg beforehand. This helps one to understand the pattern of the varicosities and is also a permanent record (fig. 2). The results are somewhat variable and depend on the thickness of the patient's skin and the amount of subcutaneous fat.

Operation

Under general anæsthesia the skin of the whole leg is cleaned; the foot is towelled separately, so that the whole leg can be freely moved and veins on the back of the calf reached without turning the patient over.

For the high ligation a transverse incision is preferred to the vertical one, which, though affording better access

* Hartley's ink is one of a number of inks sold for marking garden labels. It produces a thick black mark that is insoluble in water or in spirit. Dr. W. A. Gillespie, who kindly carried out some bacteriological tests, found it sterile on culture on aerobic and anaerobic blood-agar and in broth.

DR. GEFFEN AND OTHERS: REFERENCES

Anderson, G. W., Skaar, A. E. (1951) *Pediatrics*, **7**, 741.
Bousfield, G. (1950) *Med. Offr*, **84**, 29.
Geffen, D. H. (1950) *Ibid*, **83**, 137.
Gray, P. G., Cartwright, A. (1952) *Mon. Bull. Minist. Hlth Lab. Serv.* **11**, 26.
Hill, A. B., Knowelden, J. (1950) *Brit. med. J.* ii, 1.
Korns, R. F., Albrecht, R. M., Locke, F. B. (1952) *Amer. J. publ. Hlth*, **42**, 153.
Logan, W. P. D. (1952) *Mon. Bull. Minist. Hlth Lab. Serv.* **11**, 147.
MacCallum, F. O. (1950) *Brit. med. J.* ii, 6.
McCloskey, B. P. (1950) *Lancet*, i, 659.
—— (1952) *Ibid*, i, 1187.
Martin, J. K. (1950) *Arch. Dis. Childh.* **25**, 1.
Smalipeice, V., Ounsted, C. (1952) *J. Neurol. Psychiat.* **15**, 13.
Wright, G. A., Owen, T. K. (1952) *Brit. med. J.* i, 800.

for ligation of tributaries, does not heal well. The internal saphenous vein is divided and tied flush with the femoral vein. Its terminal tributaries are sought and divided.

Ligatures are now placed down the leg at the points previously marked. Braided nylon is most suitable for this purpose, because it is non-absorbable and produces no reaction in the tissues. It is softer than monofilamentous nylon and leaves a knot which is in most cases impossible to feel under the skin later. "Six-pound" braided nylon used double is sufficiently strong.

A nick is made in the skin through two companion dots with a tenotome or narrow-ended blade such as the standard no. 11 blade. If the axis of the nick is made along Langer's lines it remains almost invisible, but it may gape if made at right-angles to it. A large $^1/_2$-circle needle—e.g., Bonney's no. 1—is threaded with braided nylon and held on a strong needle-holder (fig. 3). It is now passed, blunt end first, through one nick, under the vein, and out of the other nick, leaving the ligature in its track. It is then reinserted, blunt end first, through the second nick and passed, under the skin but over the vein, to emerge through its original point of entry, from which the two ends of the ligature are now left protruding. These are pulled backwards and forwards once or twice to enable the ligature to slip through the fat close to the vein—if it is not round the vein it will slip out altogether—and tied tightly with three hitches. The ends are cut off with a knife close to the knot. This leaves the skin puckered up, with the knot just below the puncture. If this pucker is now straightened out by stretching the skin, the knot disappears under the skin and the vein resumes its previous position half-way between the two dots. Occasionally a vein may be torn in this process and blood oozes from a puncture; this is controlled with digital pressure and ceases when the next ligature has been tied. The average number of ligatures used per limb in 50 cases was 11, and the largest number 28.

Fig. 1—Infra-red photograph showing method of marking veins. (Varicose anterior femoral cutaneous vein was missed.)

No dressings are needed except in the groin, and a sterile crêpe bandage is applied to the leg.

Results

Two or three days after the operation a clot can be felt in most cases in the isolated segments of the vein between the ligatures. Patients are ambulant from the start and are usually fit to go home the day after operation; but in the present series they were kept in hospital longer for close observation. Occasionally a mild inflammation has developed round a knot but in no case has this been severe, and the great majority of patients have no reaction beyond a vague tenderness, a little local œdema, and perhaps bruising.

Degree of Obliteration Achieved

In 64% the primary obliteration was regarded as complete without the help of any injections—i.e., all visible varices had disappeared.

Fig. 2—Pattern of varicose veins elucidated by infra-red photography.

In 30% slight varicose veins remained; in half they were negligible, and in half injections were needed to complete the obliteration.

In 6% (3 cases) the varicosities remaining when seen fourteen, thirteen and five months after operation were more than could be obliterated by injections alone. However, the patients were symptomatically relieved, and no further treatment was advised. It must also be said that 2 of the 3 in this group were in the first 5 to be treated; had they appeared later in the series, the veins would have been ligated at more points, perhaps with better results.

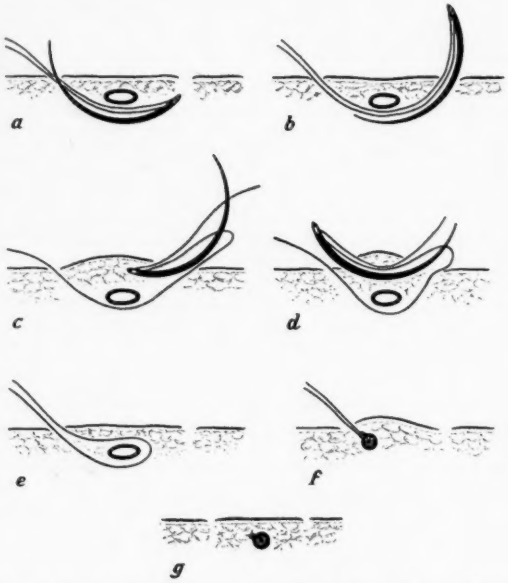


Fig. 3—Method of inserting subcutaneous ligatures (for description, see text).

In only 6 of 47 patients whose veins have been satisfactorily obliterated was it necessary to inject sclerosants.

Death from Pulmonary Embolus

It must be recorded that there was 1 death from pulmonary embolus. This occurred on the sixth post-operative day. Clotting had taken place in all the varices and had extended from one on the back of the calf, along a communication through the soleus muscle to the posterior tibial vein, and thence to the popliteal and femoral veins.

The possibility of this catastrophe seems inseparable from the intentional clotting of blood in the veins of a patient's legs. Nevertheless it seems to happen more often with some methods than with others, and retrograde injections of large amounts of sclerosants and extensive operations seem to carry the greatest risk. Thus Faxon and Barrow (1938) record 3 pulmonary emboli, 2 of which were fatal, in 228 cases of high ligation with retrograde injection; and Moore and Knapp (1942) reported 2 fatalities from this cause in 88 cases in which excisions had been done.

Whether the present method will be found to carry an undue liability to pulmonary embolus remains to be seen. On theoretical grounds it should not, because the use of sclerosants at operation is avoided and the patients can be fully ambulant immediately after operation. A patient in a hospital ward, though officially ambulant, has nothing to do to keep him on the move, and, though not actually in bed, tends to be equally immobile in an armchair. Probably the best prophylactic against pulmonary embolus is to get the patient home the day after operation.

Effect of the Knots Remaining under Skin

In the first 6 cases strong thread was used for the ligatures; most of these knots have since been discharged, some of them many months after operation, leaving a pigmented mark. In the next 4 cases fine thread was used; this has so far caused no trouble but was given up for nylon, which is very satisfactory. At first monofilamentous nylon was used, but since strong braided nylon has been available it has been preferred. Some of the monofilamentous nylon knots were palpable under the skin, and in 2 cases the patient complained of a knot, which was therefore removed.

Since braided nylon has been used, there has been no trouble. The patient is unaware of the knots which cannot be felt under the skin, and no knots have been spontaneously discharged.

Accidental Ligation of a Cutaneous Nerve

In view of the close relationship of the saphenous nerve to the vein in the leg, it might be expected that it would often be caught in a ligature. This has happened in 4 cases and has produced a small area of anæsthesia above the medial malleolus. Only 1 of these patients volunteered the information; the 3 others had not noticed it or did not think it worth mentioning.

Where large clusters of veins have been found they have been excised, and occasionally the internal saphenous vein is so large and tortuous that it is best excised. With these exceptions it can be said that, coupled with high ligation, multiple subcutaneous ligation has given good early results in 92% of 50 unselected cases, and that in only 14% of these were any subsequent injections needed.

The Question of Recurrence

Recurrences after operation for varicose veins are of two sorts, which might perhaps be termed true and false—the former due to recanalisation, and the latter due to dilatation of veins previously normal. As regards the former, if the knot remains tied tightly round the vein it will not permit blood to pass, even if recanalisation takes place on either side of it. If the veins are divided into short enough segments, this should prevent the points of obstruction from being bypassed by the opening up of collaterals. Perhaps, however, ligatures may partly ulcerate through the veins and, becoming embedded on one side, allow the circulation to be re-established. Recanalisation has been reported after the saphenous vein (Arthur 1944) and the femoral vein (Byrne and O'Neil 1952) have been ligated in continuity, but it is not stated what suture material was used. Recanalisation might be expected if catgut was used—Goldstone (1943) recommended catgut for his subcutaneous ligatures. It seems unlikely that recanalisation will take place when the ligatures are numerous and non-absorbable.

Where recurrence is due to dilatation of veins previously normal and is probably associated with incompetent deep and communicating veins, there can be no method of certain prevention. The best hope of keeping such recurrences at a minimum lies in careful marking and multiplicity of ligation to isolate as many communicators as possible.

Summary and Conclusions

According to McElwee and Maisel (1947) multiple ligature, coupled with high ligation, gives better end-results than do most other methods in common use for the treatment of varicose veins.

For the best results these ligatures need to be numerous.

A method is described by which a vein can be rapidly and (it is hoped) permanently ligated without making an incision. After a formal high ligation this method is used to tie the varicose veins at 2–4in. intervals down the leg.

The method appears to present the following advantages:

(1) It is thorough, in that enough ligatures to obliterate all the varicose veins can usually be made without inflicting a severe operation on the patient.

(2) Patients can walk about on the day after operation without much pain and can be sent home.

(3) The procedure is not complicated by the delayed healing and minor sepsis which may follow incisions in the leg.

(4) It leaves no visible scar.

(5) Further attendances by the patient for injections have been needed in less than a fifth of the cases.

(6) The operation takes much less time than ligation through incision.

The importance of careful marking is emphasised, and for this the assistance of infra-red photography is recommended.

I am grateful to Mr. D. G. C. Tasker and to Mr. R. V. Cooke for allowing me to operate on their cases and for their kindly and critical encouragement. I also want to thank Mr. F. A. Godman, of the department of photography, for the infra-red photographs and for his help.

REFERENCES

Arthur, H. R. (1944) *Lancet*, ii, 561.
Atlas, L. N. (1943) *Surg. Gynec. Obstet.* **77**, 136.
Babcock, W. W. (1907) *N.Y. med. J.* **86**, 153.
Byrne, J. J., O'Neil, E. E. (1952) *Amer. J. Surg.* **83**, 47.
Davat, (1837) *J. Connaissances méd. prat.* **5**, 68, 102.
Faxon, H. H., Barrow, D. W. (1938) *Surgery*, **3**, 518.
Goldstone, B. W. (1943) *Brit. med. J.* i, 753.
Kinmonth, J. B. (1948) *Proc. R. Soc. Med.* **41**, 632.
McElwee, R. S. jun., Maisel, B. (1947) *Ann. Surg.* **126**, 350.
Madelung, (1884) *Verhl. Dtsch. Ges. Chir.* **13**, 114.
Mayo, C. H. (1906) *Surg. Gynec. Obstet.* **2**, 385.
Moore, S. W., Knapp, G. M. (1942) *Ann. Surg.* **115**, 131.
Schede, M. (1877) *Berlin klin. Wschr.* **14**, 85.
Schiassi, B. (1908) *Sem. méd., Paris*, **28**, 601.
Smith, R. A. (1944) *Lancet*, ii, 141.
Tavel, E. (1904) *Korresp. Bl. schweiz. Ärz.* **34**, 617.
Unger, E. (1927) *Zbl. Chir.* **54**, 3273.

ASSESSMENT OF ADRENOCORTICAL ACTIVITY BY ASSAY OF 17-KETOGENIC STEROIDS IN URINE

J. K. NORYMBERSKI
Dr. Ing., Zürich
EMPIRE RHEUMATISM COUNCIL RESEARCH FELLOW

R. D. STUBBS
SENIOR TECHNICIAN

H. F. WEST
M.D. Lond., M.R.C.P.
PHYSICIAN IN CHARGE

SHEFFIELD CENTRE FOR THE INVESTIGATION AND TREATMENT OF RHEUMATIC DISEASES, NETHER EDGE HOSPITAL

WITH the rapidly growing realisation of the physiological significance of adrenocortical hormones, and especially since the introduction of cortisone and A.C.T.H., the need for a reliable method of estimating steroids of adrenocortical origin in the urine has become evident. We hope that the method described here will, at least in part, meet this need.

Steroids isolated from the adrenal cortex have a structural feature that distinguishes them from all other natural steroids; this consists in a particular mode of substitution of the "side-chain" (carbon atoms 17, 20, and 21). The types of this characteristic substitution so far encountered are as follows: (I) 20 : 21-glycol; (II) 20 : 21-ketol; (III) 17 : 20 : 21-triol; (IV) 17 : 21-diol-20-one (dihydroxyacetone); (V) 17 : 20-glycol; (VI) 17 : 20-ketol. Urinary steroids containing one of these six side-chains can reasonably be assumed to be of adrenocortical origin. The terms (*a*) corticosteroids, (*b*) (adreno)cortical steroids, (*c*) (adreno)cortical hormones and (*d*) corticoids will be used to denote respectively (*a*) steroids of types I–VI, (*b*) corticosteroids known to occur in the adrenal cortex, (*c*) the physiologically active cortical steroids, and (*d*) all substances showing cortical activity by any biological tests.

A well-established method of chemical characterisation of corticosteroids, originally developed in the laboratories of Reichstein and of Mason, consists in the oxidative fission of the side-chain with periodic acid, followed by the identification of volatile products (formaldehyde for types I–IV, acetaldehyde for type V) and/or of the non-volatile products. Of the latter those derived from types III and V are 17-ketosteroids. On the basis of these observations analytical procedures have been developed for the estimation of formaldehydogenic steroids (Lowenstein et al. 1946, Daughaday et al. 1948, Corcoran et al. 1950), acetaldehydogenic steroids (Butler and Marrian 1937, 1938, Cox 1952), and 17-ketogenic steroids (Talbot and Eitingon 1944, Fieser et al. 1944). Within the group of steroids known to occur in urine and in the absence of extraneous interfering material the above methods are rigidly specific. By substituting sodium bismuthate for periodate as oxidising agent, the estimation of 17-ketogenic steroids can be extended to include corticosteroids bearing a dihydroxyacetone side-chain (type IV) (Brooks and Norymberski 1952). Analytical procedures such as the estimation of reducing steroids (types II and IV) (Talbot et al. 1945, Heard and Sobel 1946) and the colour reaction of Porter and Silber (1950) for dihydroxyacetone derivatives (type IV) are less specific. No established analytical procedure for estimating substances of type VI is known to us.

Biological methods for estimating cortical hormones have been reviewed by Dorfman (1950). Of the available tests those based on the deposition of liver glycogen (Venning et al. 1946, Dorfman et al. 1946, Eggleston et al. 1946) are well suited for the quantitative micro-assay of "glucocorticoids." A similarly efficacious bio-assay of "mineralocorticoids" has been described (Tait et al. 1952, Simpson and Tait 1952). The bio-assays are of great importance for the study of substances showing hormonal activity; their application to urine, however, is of limited value, since corticoids are excreted in small quantities and very likely represent only a random fraction of the total urinary corticosteroids.

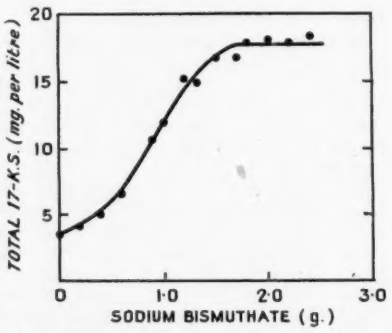


Fig. 1—Relation between quantity of sodium bismuthate and assayed "total 17-K.S."

Paper chromatography of corticosteroids has been described (Burton et al. 1951a, Bush 1952) and applied to urinary extracts (Burton et al. 1951b, Bush et al. 1952). In principle, paper chromatographic techniques offer an ideal means of separating small quantities of complex mixtures into their individual components, which can be further examined by physical or chemical methods. At present, and especially for routine purposes, chromatographic methods have not been sufficiently developed to permit a simple, comprehensive, and quantitative estimation of urinary corticosteroids.

The preparation of urinary extracts suitable for the application of any of the analytical procedures has proved most difficult, for the following reasons. Urinary corticosteroids are excreted mainly in conjugated form, demonstrably so as glucuronides and, by analogy with other urinary steroids, probably also as sulphates. Both types of conjugates are completely hydrolysed by heating with strong mineral acid; this procedure has been found reasonably satisfactory for the extraction and subsequent estimation of, for example, œstrogens, 17-ketosteroids, and pregnanediol, but unfortunately causes the destruction of many corticosteroids. Extraction of untreated urine yields only a small quantity of "free" corticosteroids; at pH1 the extracted amount is substantially increased, and a further increase is achieved by enzymatic hydrolysis with β-glucuronidase. Bayliss (1952) has compared the relative efficacy of the above extraction techniques as assayed by the formaldehydogenic method. It appears from the work of Bayliss and others (for references see Bayliss 1952) that none of the available methods will yield a urinary extract containing the total excreted corticosteroids or a constant fraction thereof which could be considered to reflect adrenocortical activity.

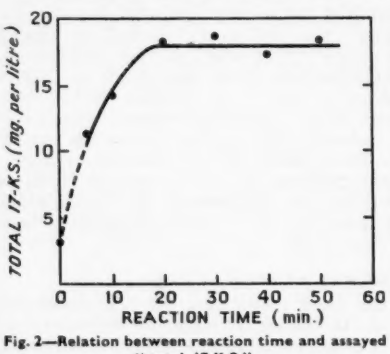


Fig. 2—Relation between reaction time and assayed "total 17-K.S."

Norymberski (1952) has shown that sodium bismuthate converts urinary 17-ketogenic steroids in situ to 17-ketosteroids; the latter can be hydrolysed, extracted, and assayed in the usual manner. Thus one group

of corticosteroids can be estimated without the usual unsatisfactory hydrolysis and extraction procedures.

The term "17-ketogenic steroids" will be used here to denote corticosteroids bearing the side-chains III, IV, or V—i.e., those converted by bismuthate (and not by periodate) into 17-ketosteroids.

Method

24-hour urine specimens are collected without preservative, made up to 2 litres with distilled water, and stored in a refrigerator. Each specimen is assayed, in duplicate, concurrently for 17-ketosteroids (17-K.S.) and for "total 17-K.S." (after bismuthate oxidation). The difference between the two measurements represents the 17-ketosteroids formed from 17-ketogenic steroids on oxidation. This figure is designated '17-K.G.S.' On a molar basis, and subject to the limitations inherent in the colorimetric determination of 17-K.S., it is a direct measure of the assayed 17-ketogenic steroids. If, as is customary, the figures for 17-K.S. and "total 17-K.S." are expressed in weight units, the resulting values of 17-K.G.S. are about 20% lower than the actual quantities of the estimated 17-ketogenic steroids.

Estimation of 17-K.S.

The following procedure is adapted from the method of Drekter et al. (1952). 12 glass-stoppered centrifuge tubes of about 30 ml. capacity are held by spring clips in an H-shaped metal frame. From each of six specimens two 8-ml. aliquots are placed in the tubes, and 2 ml. glacial acetic acid and 3 ml. concentrated hydrochloric acid are added to each tube. The rack of tubes is kept in a boiling water-bath for 10 minutes, then cooled in cold water; to each tube 10 ml. ethylene dichloride (purified by shaking with concentrated sulphuric acid and redistilled) is added; the tubes are stoppered and shaken mechanically (in the rack) for 15 minutes. The stoppers are now removed, the tubes centrifuged, and the aqueous phases removed with suction. The ethylene-dichloride extracts are shaken firstly with 2·5 ml. distilled water for 2 minutes and then with 2·5 ml. 3*N* sodium hydroxide solution for 5 minutes; after each wash the layers are separated by centrifuging and the upper phases removed by suction. The washed extracts are filtered through fluted paper into test-tubes, and from each filtrate two aliquots of 2·5 ml. are transferred into smaller test-tubes (5 × 1/2 in.), evaporated on a water-bath kept just below boiling, and finally brought to dryness in vacuo and assayed by the Callow-Zimmermann method (Callow et al. 1938), as modified by Zygmuntowicz et al. (1951); a colour correction (Talbot et al. 1942a and b, Medical Research Council 1951) is applied. The colorimetric estimation is made on batches of twelve extracts; with each batch two standards of 20 μg. dehydroepiandrosterone are included, and the 17-K.S. content of the extracts is calculated from the average standard value. The conversion factor from μg. per aliquot into mg. 17-K.S. per 24 hours is 1·0.

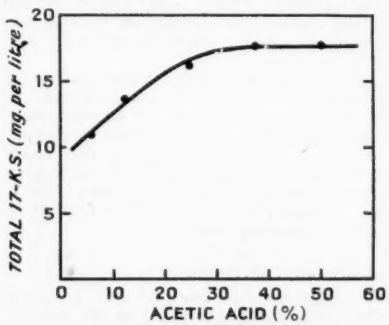


Fig. 3—Relation between concentration of acetic acid and assayed "total 17-K.S."

Estimation of "Total 17-K.S."

As in the estimation of 17-K.S. two 8-ml. aliquots are taken from each specimen and all following operations carried out on a batch of 12 tubes. To each tube 8 ml. glacial acetic acid and 2 g. sodium bismuthate ('Analar') are added. The mixtures are shaken mechanically for half an hour with exclusion of direct daylight. The stoppers are removed and the tubes centrifuged for 5 minutes at a moderate speed. From each supernatant aliquots of 10 ml. are transferred into large centrifuge tubes (approximate capacity 50 ml.); to each tube five drops of a 5% sodium hydrogen sulphite solution and 10 ml. distilled water are added, the mixtures are stirred with a glass rod, treated with 6 ml. concentrated hydrochloric acid, and stirred again. The hydrolysis and all following operations are performed as in estimating 17-ketosteroids, but using 20 ml. ethylene dichloride for extraction and 5 ml. water and 5 ml. 3*N* sodium hydroxide solution for washing. Of the final extracts two aliquots of 5 ml. are taken for the colorimetric estimations. The conversion factor into mg. "total 17-K.S." per 24 hours is 1·6.

TABLE I—COMPARISON OF ORIGINAL AND MODIFIED METHOD

Experimental detail	"Total 17-K.S." (mg. per litre)	d_{440}/d_{420}
Treatment with NaOH pellets (Original method)	11·2	1·0
	11·8	1·0
	8·8	1·0
	9·3	0·9
	14·1	1·1
	12·8	1·1
As above with added $NaHSO_3$	16·4	1·2
	14·7	1·1
Treatment with aqueous alkali	9·8	1·5
	8·7	1·6
	8·4	1·5
	10·3	1·7
	9·7	1·5
As above with added $NaHSO_3$ (Present method)	16·8	2·2
	16·6	2·0
	18·0	2·0
	16·4	1·8
	16·2	1·9

VARIATION OF EXPERIMENTAL CONDITIONS

Quantity of Sodium Bismuthate

Apart from corticosteroids other urinary constituents—e.g., sugars—must be expected to react with sodium bismuthate, hence a large excess of the reagent will be necessary for the quantitative oxidation of urinary corticosteroids in situ. Fig. 1 clearly shows that, for the investigated urine specimen, the quantity of sodium bismuthate used in the standard procedure is in fair excess of that necessary

TABLE II—RECOVERY OF MODEL SUBSTANCES ADDED TO URINE

Type	Substance added	μg. of (*b*) per ml.	17-ketosteroid formed	Colour equiv. of (*d*)	Increase of "total 17-K.S." (μg. per ml.)		% recovery
					Calc.	Found	
(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*f*)	(*g*)	(*i*)
III	17α: 20β: 21-Trihydroxypregn-4-en-3-one	14·5	Androst-4-ene-3: 17-dione	119	14·1	13·3	94
IV	17α-Hydroxy-11-dehydrocorticosterone (cortisone)	15·4	Androst-4-ene-3: 11: 17-trione	93	12·0	9·5	79
IV	17α-Hydroxycorticosterone (Kendall's Compound F)	12·5	11β-Hydroxyandrost-4-ene-3: 17-dione	66	6·9	5·8	84
V	3α: 17α: 20β-Trihydroxypregnan-11-one	14·7	3α-Hydroxyetiocholane-11: 17-dione	118	15·1	12·8	85

Column (*e*): expressed in μg. dehydroepiandrosterone per 100 μg. 17-ketosteroid.

Column (*f*): calculated value = $\frac{\text{molecular weight of } (d) \times (c) \times (e)}{\text{molecular weight of } (b) \times 100}$.

to complete the oxidation. With other urines we have repeatedly observed that the use of larger quantities of the reagent (over 2 g.) does not significantly affect the results of the estimations.

Time of Reaction

Fig. 2 shows the relation between the reaction time and the assayed "total 17-K.S." 30 minutes appears to be a suitable reaction time for the standard procedure.

Concentration of Acetic Acid

While pure 17-ketogenic steroids are quantitatively convertible to 17-ketosteroids on oxidation with sodium bismuthate in 1–5% acetic acid (Brooks and Norymberski 1952), it appears that the oxidation in situ of urinary corticosteroids requires a much higher concentration of acetic acid (see fig. 3). Furthermore, we find that in the presence of 10% acetic acid only 60% of added dehydroepiandrosterone is recovered from urine submitted to treatment with sodium bismuthate, whereas in the presence of 50% acetic acid the recovery exceeds 90%. These observations may be explained if it is assumed that steroids are adsorbed on the surface of sodium bismuthate. At low concentrations of acetic acid, and in the presence of large quantities of the reagent, necessary for the oxidation in situ but not for the oxidation of pure substances, the quantity adsorbed can be expected to increase.

Other Changes of Experimental Conditions

The estimation procedure in initial experiments (Norymberski 1952) differed in two respects from that now reported: (1) the ethylene dichloride extracts were treated with sodium hydroxide pellets as recommended by Drekter et al. (1952);

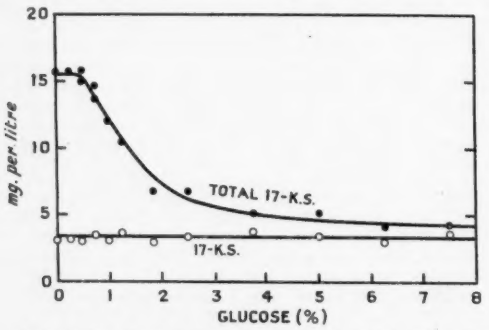


Fig. 4—Inhibition by glucose of oxidation of urinary 17-ketogenic steroids.

(2) no sodium hydrogen sulphite was added after oxidation and before hydrolysis. For a time the original method was considered satisfactory, judging by the agreement between separate estimations and by the ratios of optical densities (d) at wave-lengths 520 mμ and 430 mμ (Talbot et al. 1942a). Occasionally, however, a series of estimations was found to give results which, by both criteria, were unsatisfactory. Furthermore, when it became possible to calculate more accurately the recoveries of pure 17-ketogenic steroids added to urine, the recovery figures were found to be rather low. The source of the erratic results was finally traced to the treatment with sodium hydroxide pellets and to the presence of an oxidising agent in the supernatant of the urine/acetic-acid/bismuthate mixture. By substituting for the pellet treatment a conventional aqueous alkali wash, and by reducing the soluble oxidant with sodium hydrogen sulphite, the following improvements were achieved: (1) more consistent results of separate estimations, (2) increased ratios of d_{520}/d_{430}, and (3) higher values for estimated "total 17-K.S." Table I illustrates these improvements in a series of experiments which by the original method gave particularly bad results. Similar, though less striking, improvements were observed in other experiments designed to compare the original with the present method. The greater efficacy of the latter is further demonstrated by the improved recoveries of corticosteroids added to urine.

RECOVERY OF 17-KETOGENIC STEROIDS ADDED TO URINE

Norymberski (1952) recorded the recoveries of corticosteroids representing types III, IV, and V. Since then the technique of the estimation has been improved, and Zimmermann colour equivalents have been determined for 17-ketosteroids derived from model substances used in the recovery experiments. We have therefore repeated the recovery experiments (table II).

Wilson (1950) has previously shown that individual 17-ketosteroids can differ considerably in the colour intensities developed with the Zimmermann reagent. It was necessary to repeat this work because (1) our colorimetric technique differs from that employed by Wilson, and (2) the colour equivalents of several substances relevant to our work were not recorded. Apart from the colour equivalents listed in table II, column (*e*), those of various other ketosteroids have been determined and will be reported elsewhere.

TABLE III—EXCRETION OF 17-K.S. AND 17-K.G.S. IN NORMAL ADULTS AND CHILDREN

Subject	Sex	Age (yr.)	mg. per 24 hr.	
			17-K.S.	17-K.G.S.
ST/1	M	24	18·2	9·6
ST/2			15·4	9·7
BR	M	25	15·0	15·6
CR	M	25	19·2	19·2
NW	M	36	14·0	15·7
MT	M	51	10·2	10·0
HW	M	52	14·6	13·2
SQ	M	64	15·3	12·2
WH	F	19	14·6	9·4
KP	F	19	8·0	7·0
MD	F	19	9·8	10·0
GR	F	26	15·6	4·6
CS	F	39	12·6	7·4
CR	F	44	5·2	7·8
RH	F	51	4·8	12·8
MR	F	51	5·6	13·4
GR	F	53	4·8	7·6
EM	M	6	1·3	2·9
WL	M	6	0·9	2·3
JH	F	6	1·1	2·3
DD	F	6	0·9	3·4
EM	F	8	1·4	2·8
WS	F	11	3·5	3·8

INHIBITION BY GLUCOSE

The experimental conditions laid down in the preceding paragraphs have been found satisfactory in over 200 urinary assays, many of which were checked by the recovery of added pure 17-ketogenic steroids or by varying the quantity of sodium bismuthate. Occasionally, however, it may be necessary to assay a specimen with an abnormally high glucose content which could vitiate the determination. To test the extent of such interference estimations of 17-K.S. and "total 17-K.S." were carried out on a specimen to which glucose had been added in quantities varying from 0·25 to 7·5%. The results, recorded in fig. 4, show that with more than 0·5% glucose the estimated "total 17-K.S." are significantly decreased. It is therefore important to test for

TABLE IV—EXCRETION OF 17-K.S. AND 17-K.G.S. IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, OR STILL'S DISEASE

Subject	Sex	Age (yr.)	Disease	mg. per 24 hr.	
				17-K.S.	17-K.G.S.
KN	M	27	Ank. spond.	7·0	6·2
HW	M	37	,, ,,	10·0	6·1
TH	M	45	,, ,,	21·4	12·8
BR*	M	38	Rh. arth.	7·3	7·5
SM*	M	52	,, ,,	7·1	7·3
HL	M	55	,, ,,	7·6	8·4
BR	M	60	,, ,,	4·8	8·4
SV	F	22	,, ,,	10·4	10·8
BR	F	31	,, ,,	7·3	8·5
SM	F	39	,, ,,	4·6	5·4
DN	F	43	,, ,,	6·6	6·6
BL	F	46	,, ,,	10·8	4·2
MR	F	47	,, ,,	6·1	5·7
GL	F	51	,, ,,	5·0	3·1
PR	F	54	,, ,,	4·2	3·8
CT/1	F	54	,, ,,	4·0	3·0
CT/2				4·9	3·8
SC*	F	59	,, ,,	4·8	2·2
HW/1	F	60	,, ,,	16·4	6·3
HW/2				19·2	9·2
WH	F	62	,, ,,	4·5	3·1
WH	F	3	Still's	0·8	1·2
TR	F	12	,,	3·5	8·6

* On phenylbutazone treatment.

the presence of glucose (e.g., with Benedict's solution) before carrying out the estimation of 17-K.G.S. The problem of assaying specimens with a high glucose content may be approached either by increasing the amount of sodium bismuthate or by attempting to remove the glucose prior to estimation.

Results of Assays

Some of the results given here can be confidently accepted for interpretation, while others require additional data to make statistically sound generalisations possible. Whenever several specimens of one subject were assayed, estimations of creatinine were carried out as well. The latter are recorded only for the one case in which they were found erratic.

Normal Adults and Children

From the figures in table III no relation is apparent between the excretion of 17-K.G.S. and the age of the adults. There seems to exist, however, a difference between the 17-K.G.S. levels of men and women, the latter being, on the average, about 30% lower.

TABLE V—EXCRETION OF 17-K.S. AND 17-K.G.S. IN VARIOUS CONDITIONS

Subject	Sex	Age (yr.)	Condition	mg. per 24 hr.	
				17-K.S.	17-K.G.S.
			Pregnancy :		
CR	F	24	4th month	11·3	6·4
ML	F	20	7th ,,	10·3	8·9
CD	F	20	9th ,,	16·0	8·2
MN	F	28	5th month plus Addison's dis.	3·2	3·2
			Operation :		
FX/1	M	71	Before (*a*)	6·0	20·2
FX/2			After	11·6	55·2
BC/1	M	56	Before (*b*)	10·8	15·8
BC/2			After	16·0	20·8
BT/1	M	47	Before (*c*)	6·8	6·8
BT/2			After	13·6	14·6
PR/1	F	49	Before (*d*)	4·4	1·8
PR/2			After	7·8	26·2
SH	F	66	Simmonds's dis.	nil	2·0
CH	F	65	Cushing's syn.	9·3	14·8

(*a*) Prostatectomy. (*b*) Excision of sacrococcygeal sinus. (*c*) Partial gastrectomy. (*d*) Partial colectomy.

Rheumatoid Disease and Ankylosing Spondylitis

Patients with rheumatoid arthritis or ankylosing spondylitis show considerably lower 17-K.G.S. levels (average about 40%) than normal adults (table IV). Whether this finding is characteristic of these diseases or is simply due to the inactivity that they impose remains to be shown. Within this group, as among normal adults, the same relation is discernible between excreted 17-K.G.S. and the sex of the subjects. Treatment with moderate doses of salicylate or phenylbutazone does not appear to affect the output of 17-K.G.S.

Other Conditions

In three cases of pregnancy the 17-K.G.S. figures were found to fall within the normal range (table V). This is of some interest since: (1) amelioration of rheumatoid arthritis during pregnancy (Hench 1938) could tempt one to postulate an increased adrenal output of 17α-hydroxycorticosterone (Kendall's Compound F) in this condition; and (2) Venning (1946) reported an increased excretion of corticoids (assayed by the liver glycogen test) in pregnancy. Urines from patients after operation show, as expected, greatly increased 17-K.G.S. values.

Treatment with Cortisone Acetate

The excretion of 17-K.S. and 17-K.G.S. in a normal male aged 42 was estimated at short intervals for 24 hours before and after a single oral dose of 100 mg. cortisone acetate. The excretion-rate is graphically recorded in fig. 5. The output of 17-K.G.S. returns to normal after 16 hours; about 50% of the total increase is excreted within the first 4 hours, and about 75% within 8 hours. This rate of excretion roughly corresponds to the commonly observed period of clinical effectiveness of a single large oral dose.

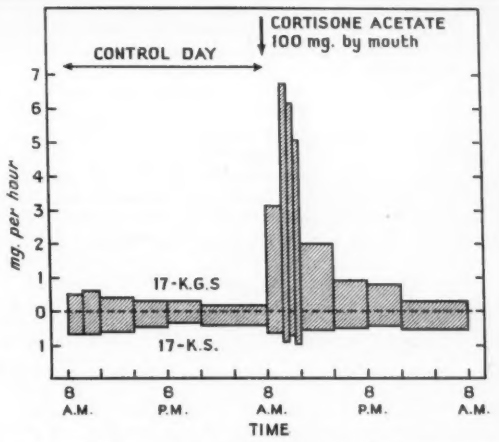


Fig. 5—Excretion-rate of 17-K.G.S. and 17-K.S. after administration of cortisone acetate by mouth.

Results of assays on patients receiving between 12·5 mg. and 100 mg. cortisone acetate daily clearly show proportionality between dose and 17-K.G.S. levels (table VI). The graphic representation (fig. 6) exhibits, for doses over 37·5 mg., a straight line passing through the origin. We tentatively conclude that oral doses of about or above 37·5 mg. cortisone acetate can almost completely suppress the endogenous production of 17-ketogenic steroids. It is interesting to note that this figure corresponds with the minimum dose that produces benefit in rheumatoid arthritis.

TABLE VI—EXCRETION OF 17-K.S. AND 17-K.G.S. IN PATIENTS UNDER TREATMENT WITH CORTISONE ACETATE

Subject	Sex	Age (yr.)	Disease	Day of treatment	Cortisone acetate by mouth (mg. per day)	mg. per 24 hr.	
						17-K.S.	17-K.G.S.
BV/1	M	45	Rh. arth.	52	75·0	6·8	30·2
BV/2				60	75·0	9·6	31·4
BV/3				73	75·0	8·0	28·8
BV/4				101	75·0	6·6	32·0
BV/5				111	75·0	6·4	29·8
BV/6				125	75·0	7·0	28·2
BV/7				143	75·0	6·2	23·2
LM/1	M	30	Ank. spond.	74	75·0	8·6	27·4
LM/2				97	75·0	10·2	29·2
LM/3				101	75·0	8·2	28·0
ES	M	36	Rh. arth.	113	75·0	10·4	35·6
SP	F	40	,, ,,	30	75·0	5·4	24·4
MR/1	F	26	Ank. spond.	365	62·5	4·4	24·4
MR/2				374	62·5	3·2	24·8
TT	F	29	Rh. arth.	39	62·5	5·2	19·6
RB	F	37	,, ,,	729	62·5	4·0	28·6
PR	F	52	,, ,,	46	50·0	6·2	19·6
RG	F	47	,, ,,	276	50·0	4·6	18·6
PR	F	52	,, ,,	23	37·5	5·2	14·4
TR	F	12	Still's	2	37·5	5·0	14·0
BR/0	F	31	Rh. arth.	0	0·0	8·2	6·2
BR/1				1	12·5	8·0	8·8
BR/2				2	12·5	7·6	9·4
BR/3				3	25·0	7·0	12·8
BR/4				4	25·0	8·6	11·6
BR/5				5	37·5	5·8	13·4
BR/6				6	37·5	9·0	15·1
BR/7				7	50·0	5·0	19·2
BR/8				8	50·0	6·3	21·7
BR/9				9	50·0	6·8	22·2
BR/10				10	62·5	6·4	26·8
BR/11				11	75·0	7·4	30·2
BR/12				12	75·0	8·4	29·6
BR/13				13	87·5	7·0	37·8
BR/14				14	87·5	4·9	33·9
BR/15				15	87·5	5·0	30·8
BR/16				16	100·0	4·6	39·2
BR/17				17	87·5	5·0	35·0

The gradient in fig. 6 expresses the recovery of 17-K.G.S. in terms of mg. dehydroepiandrosterone per mg. cortisone acetate. The percentage recovery is 40. Assuming that "tetrahydrocortisone" is the main urinary 17-ketogenic steroid derived from cortisone a correction must be made for the Zimmermann equivalent (118) of the actually determined substance—3α-hydroxyetiocholane-11 : 17-dione (see table II). Furthermore, to arrive at the theoretical recovery (mole per mole) the molecular weights of cortisone acetate (402·5) and of 3α-hydroxyetiocholane-11 : 17-dione (304·4) have to be considered. Thus the percentage recovery is

$$\frac{40 \times 402{\cdot}5 \times 100}{118 \times 304{\cdot}4} \approx 45\%$$

of the theoretical amount. By a similar calculation, and with the additional assumption that 17-ketogenic steroids

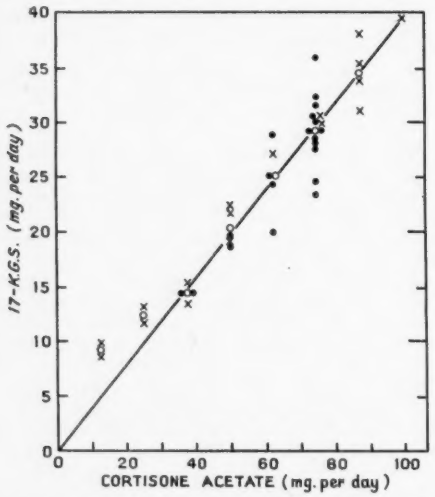


Fig. 6—Relation between dose of cortisone acetate by mouth and assayed 17-K.G.S. Crosses = specimens BR/0 to BR/17 (table VI). Closed circles = all other specimens in table VI. Open circles = mean values for all assays on same dose.

secreted by the adrenal are metabolised in the same way as orally administered cortisone acetate, the daily adrenal output of 17-ketogenic steroids may be approximated from the excretion of 17-K.G.S. in untreated subjects. Taking the average daily excretion of normal men (13·5 mg.) and women (9·0 mg.) the calculated adrenal secretion figures are 30 mg. and 20 mg. respectively. Considering the speculative character of this calculation it is remarkable how well the above figures agree with the doses of 25 to 50 mg. cortisone given in substitution therapy of bilaterally adrenalectomised patients (Huggins and Bergenstal 1951, Pearson et al. 1952, Thorn et al. 1952).

Treatment with A.C.T.H.

In the majority of cases investigated by us treatment with A.C.T.H. caused striking increases of excreted 17-K.G.S.; their magnitude, however, varied greatly with the subject (table VII).

Fig. 7 records the excretion of 17-K.G.S. and 17-K.S. for a rheumatoid patient on 60 units 'Acthar Gel' per day over a period of 2 weeks : both 17-K.G.S. and 17-K.S. rose gradually during the first 10 days of treatment, and fell on the 13th day to a level which after a further week of treatment was found practically unchanged (table VII, subject BR).

The results of an experiment designed to test the response of the adrenal to stimulation by A.C.T.H. during prolonged treatment with cortisone are recorded in fig. 8. A man, aged 29, with very severe ankylosing spondylitis, who had been treated with 75 mg. cortisone acetate daily for more than 2 months, was given in addition acthar gel 30 units 12-hourly for 2 days. The adrenal response in this case is clearly demonstrated by the considerable increase of 17-K.G.S.; further distinct clinical improvement was also apparent.

TABLE VII—EXCRETION OF 17-K.S. AND 17-K.G.S. IN PATIENTS UNDERGOING TREATMENT WITH ACTHAR GEL

Subject	Sex	Age (yr.)	Disease	Day of treatment	Acthar gel (I.U. per day)	mg. per 24 hr.	
						17-K.S.	17-K.G.S.
WL	F	34	Rh. arth.	34	20	8·8	19·6
SX	F	41	,, ,,	87	30	9·6	12·2
LM/1	M	38	,, ,,	25	40	19·2	25·6
LM/2				32	40	25·7	42·0
ES/1	M	36	,, ,,	18	40	4·8	10·2
ES/2				24	40	6·7	13·9
ES/3				28	40	6·7	13·8
KN/1	M	35	Ank. spond.	245	50	43·4	61·8
KN/2				265	50	39·8	49·8
BR	M	38	Rh. arth.	22	60	15·2	23·0

Conclusions

In recent years evidence has been gained indicating that 17α-hydroxycorticosterone (Kendall's Compound F) is the main cortical steroid secreted into the bloodstream of man (Nelson and Samuels 1952) and other higher animals (Hechter 1950, Reich et al. 1950, Bush 1951, Savard et al. 1952). On the other hand, Baggett et al. (1952) have shown that "tetrahydrocortisone," a likely metabolite of 17α-hydroxycorticosterone, is the principal urinary corticosteroid in normal adults and pregnant women. Furthermore Romanoff et al. (1952) have isolated from human urine about twenty steroids : of the six which have been identified all proved to be dihydroxyacetone derivatives (type IV)—i.e., substances falling within the group of 17-ketogenic steroids. Our finding of a linear relation between dose of administered cortisone acetate and quantity of excreted 17-K.G.S. leads us therefore to believe that the assay of the latter constitutes a measure of adrenal activity, or more precisely that part of it which is concerned with the production of 17α-hydroxycorticosterone. Determination of 17-K.G.S. does not include 17-desoxy compounds (types I and II); hence no information about the secretion of corticosterone can be derived from it.

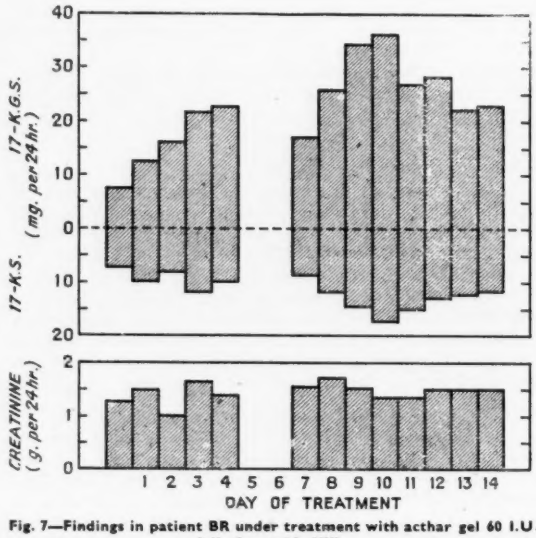


Fig. 7—Findings in patient BR under treatment with acthar gel 60 I.U. daily (see table VII).

As compared with other methods of estimating urinary corticosteroids the assay of 17-K.G.S. offers obvious advantages: (1) the difficult and unsolved problem of preparing a urine extract suitable for quantitative determination of corticosteroids is circumvented, (2) a reasonable degree of reproducibility and reliability is achieved, and (3) the assay appears to provide an index of a particular function of the adrenal—its release of 17α-hydroxycorticosterone. A further advantage of some practical importance is the simplicity of the method: it requires very little more time and only one more operational stage than the customary estimation of 17-ketosteroids.

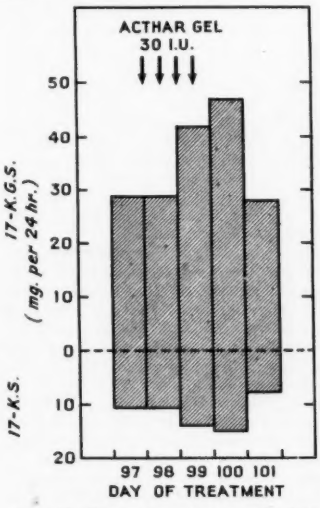


Fig. 8—Findings in a patient on the 97th–101st days of treatment with cortisone acetate, 75 mg. per day, with acthar gel 60 I.U. per day on the 98th and 99th days.

Summary

A method is described for determining a structurally well-defined group of urinary corticosteroids designated 17-ketogenic steroids.

The 24-hour excretion of 17-ketogenic steroids was found to be 9·6–19·2 mg. for normal men, 4·6–13·4 mg. for normal women, and 2·3–3·8 mg. for normal children (aged 6–11 years, both sexes).

In patients with rheumatoid arthritis the average daily excretion was about 40% below normal values. In patients with rheumatoid arthritis who were being treated with cortisone acetate by mouth there was a linear relation between the figures for dose and excretion. In patients with rheumatoid arthritis who were being treated with A.C.T.H. there was increased excretion of 17-K.G.S., varying irregularly with dose and subject. In patients who had lately undergone surgical operations excretion was greatly increased. In pregnant women the level of excretion was within normal range.

After administration of cortisone acetate by mouth about 50% of the increased 17-ketogenic steroids was excreted in the first 4 hours.

The daily adrenal output of 17-ketogenic steroids, probably expressing mainly the secretion of 17α-hydroxycorticosterone, is calculated to be about 30 mg. for normal men and 20 mg. for normal women.

We are indebted to Mr. G. Gibson for his skilful assistance in many of the estimations, and to Mr. B. H. Williams for the creatinine determinations. We further wish to thank all those who have provided 24-hour urine specimens: especial thanks are due to Sister R. S. MacLaurin who was responsible for the collections in our wards. Acknowledgment is made of gifts of steroids from British Schering, Ltd., Merck & Co., Inc., and N. V. Organon (Oss.). Finally we thank Dr. C. J. W. Brooks for discussions on various aspects of this work, and for help with the manuscript.

REFERENCES

Baggett, B., Glick, J. H. jun., Kinsella, R. A. jun. (1952) *J. clin. Invest.* **31**, 616.
Bayliss, R. I. S. (1952) *Biochem. J.* **52**, 63.
Brooks, C. J. W., Norymberski, J. K. (1952) *Chem. & Ind. (rev.)*, p. 804.
Burton, R. B., Zaffaroni, A., Keutman, E. H. (1951a) *J. biol. Chem.* **188**, 763.
— — — (1951b) *Ibid*, **193**, 769.

References continued at foot of next column

THIOURACIL IN PREGNANCY
ITS EFFECT ON THE FŒTUS

NORAH ELPHINSTONE
M.B. Lond., D.C.H.
LATE PÆDIATRIC REGISTRAR, WHITTINGTON HOSPITAL, HIGHGATE, LONDON

SINCE Astwood (1943) first reported the clinical use of thiourea and thiouracil, these drugs have commonly been used in the treatment of thyrotoxicosis, but their use during pregnancy and lactation may harm the fœtus and newborn infant.

Maternal thyroid hormone, which diffuses across the placenta, normally controls the development of the fœtal thyroid gland (Caren 1949). Hughes (1944) found that thiouracil or its derivatives, given to pregnant rats, led to hyperplasia of the thyroid gland in the offspring. This disappears if the drug is discontinued immediately after birth (Freiesleben and Kjerulf-Jensen 1946). Thyroid hyperplasia is also produced by feeding thiouracil to young rats, but disappears when a normal diet is given (Goldsmith et al. 1945). Hughes (1944) and Freiesleben and Kjerulf-Jensen (1946) both demonstrated that if young rats imbibed the milk of thiouracil-treated mothers the thyroid hyperplasia increased, growth was retarded, and cretinism was eventually produced. As thiouracil is excreted in the milk of thiouracil-treated women (Williams et al. 1944), the same fate might overtake the human infant.

Freiesleben and Kjerulf-Jensen (1947) proved that thiouracil derivatives pass across the placenta from mother to fœtus, and found that the thyroid hyperplasia, generally produced by the administration of methylthiouracil to infant rats, could be prevented by the concurrent administration of thyroid hormone, showing

DR. NORYMBERSKI AND OTHERS: REFERENCES—*continued*

Bush, I. E. (1951) *J. Endocrin.* **7**, lxxxiii.
— (1952) *Biochem. J.* **50**, 370.
— de Courcy, C., Gray, C. H. (1952) *J. Endocrin.* **8**, xii.
Butler, G. C., Marrian, G. F. (1937) *J. biol. Chem.* **119**, 565.
— — (1938) *Ibid*, **124**, 237.
Callow, N. H., Callow, R.K., Emmens, C. W. (1938) *Biochem. J.* **32**, 1312.
Corcoran, A. C., Page, I. H., Dustan, H. P. (1950) *J. Lab. clin. Med.* **36**, 297.
Cox, R. I. (1952) *Biochem. J.* **52**, 339.
Daughaday, W. H., Jaffe, H., Williams, R. H. (1948) *J. clin. Endocrin.* **8**, 166.
Dorfman, R. I. (1950) *In* Hormone Assay, edited by C. W. Emmens. New York; p. 325.
— Ross, E., Shipley, R. A. (1946) *Endocrinology*, **38**, 178.
Drekter, I. J., Heisler, A., Scism, G. R., Stern, S., Pearson, S., McGavack, T. H. (1952) *J. clin. Endocrin.* **12**, 55.
Eggleston, N. M., Johnston, B. J., Dobriner, K. (1946) *Endocrinology*, **38**, 197.
Fieser, L. F., Fields, M., Lieberman, S. (1944) *J. biol. Chem.* **156**, 191.
Heard, R. D. H., Sobel, H. (1946) *Ibid*, **165**, 687.
Hechter, O. (1950) *Fed. Proc.* **9**, 58.
Hench, P. S. (1938) *Proc. Mayo Clin.* **13**, 161.
Huggins, C., Bergenstal, D. M. (1951) *J. Amer. med. Ass.* **147**, 101.
Lowenstein, B. E., Corcoran, A. C., Page, I. H. (1946) *Endocrinology*, **39**, 82.
Medical Research Council (1951) *Lancet*, ii, 585.
Nelson, D. H., Samuels, L. T. (1952) *J. clin. Endocrin.* **12**, 519.
Norymberski, J. K. (1952) *Nature, Lond.* **170**, 1074.
Pearson, O. H., Hollander, V. P., West, C. D., Whitmore, W. F., Randall, H. T. (1952) *J. clin. Invest.* **31**, 653.
Porter, C. C., Silber, R. H. (1950) *J. biol. Chem.* **185**, 201.
Reich, H., Nelson, D. H., Zaffaroni, A. (1950) *Ibid*, **187**, 411.
Romanoff, L. P., Wolff, R. S., Pincus, G. (1952) *Fed. Proc.* **11**, 131.
Savard, K., Koiff, W. J., Corcoran, A. C. (1952) *Endocrinology*, **50**, 366.
Simpson, S. A., Tait, J. F. (1952) *Ibid*, p. 150.
Tait, J. F., Simpson, S. A., Grundy, H. M. (1952) *Lancet*, i, 122.
Talbot, N. B., Berman, R. A., McLachlan, E. A. (1942a) *J. biol. Chem.* **143**, 211.
— — — (1942b) *Ibid*, **144**, preceding p. 571.
— Eitingon, I. V. (1944) *Ibid*, **154**, 605.
— Saltzman, A. H., Wixom, R. L., Wolfe, J. K. (1945) *Ibid*, **160**, 535.
Thorn, G. W., Harrison, J. H., Merril, J. P., Criscitiello, M. G., Frawley, T. F., Finkenstaedt, J. T. (1952) *Ann. intern. Med.* **37**, 972.
Venning, E. H. (1946) *Endocrinology*, **39**, 203.
— Kazmin, V. E., Bell, J. C. (1946) *Ibid*, **38**, 79.
Wilson, H. (1950) *Fed. Proc.* **9**, 246.
Zygmuntowicz, A. S., Wood, M., Christo, E., Talbot, N. B. (1951) *J. clin. Endocrin.* **11**, 578.

that it is thyroid deprivation, and not a toxic effect of the drug, which harms the fœtus. They concluded that if the mother's metabolic rate is kept within normal limits, the fœtus should be unharmed, but that if the mother becomes myxœdematous, the fœtus will share the same fate. In pregnancy the metabolic rate remains at the normal level until the sixth month, and may then rise as high as +25%. Therefore, when a woman in late pregnancy is receiving thiouracil, her metabolic rate should not be allowed to fall to normal, for the mild hypothyroidism induced may result in a deficient supply of thyroid hormone to the fœtus. On the basis of experimental work, the human fœtus and suckling infant might be expected to suffer if thiouracil and related drugs are administered during pregnancy. Several reports have been published on the offspring of mothers who received thiouracil or a derivative for the whole or part of pregnancy.

PREVIOUS REPORTS

Williams (1946) treated 5 women, including 1 with a twin pregnancy. The 6 infants were healthy at birth and none had a goitre. Astwood and Vander Laan (1946) treated 3, Reveno (1948) 3, Sexton (1946) 2, Trotter (1951) at least 4, and Rose and McConnell (1944), Vogt (1946), Carns and Poser (1946), Caren (1949), Bain (1947), and Eisenberg (1950) each treated 1 case; and all these babies were normal. Palmer (1945) treated 3 women, and the only infant on which she reported fully was normal.

Whitelaw (1947) described 3 cases: only 2 carried to term, and 1 baby was normal; the other was an anencephalic monster. The weight, iodine content, and histological appearance of its thyroid gland were within normal limits.

Lahey and Bartels (1947) treated 8 pregnant women, and Mussey et al. (1948) 1, by partial thyroidectomy following preparation with an antithyroid drug. Each patient delivered a normal infant at term. Bell (1950) treated 21 pregnant women in the same way: 10 of his patients were delivered at term of 11 normal infants, who developed normally while under observation for periods ranging from eleven months to five years; 6 women had not reached term when the report was written, and 1 woman aborted. There were 2 premature deliveries, 1 of the babies being macerated, while the other was deformed and died in four hours. Another baby died at birth, and another, delivered by cæsarean section, died at six hours. The condition of the thyroid glands of these infants was not reported.

10 cases have been reported in which abnormality in the fœtus or infant was considered to be due to the passage of thiouracil through the placenta.

Davis and Forbes (1945) described the case of a woman who was taking 0·2 g. of thiouracil daily when she became pregnant. After the diagnosis of pregnancy in the second month, she took 0·2 g. on alternate days until the sixth month when she died suddenly, her death being unexplained. The fœtus had a hyperplastic and hypertrophied thyroid gland, the histological appearance being similar to that found by Donald and Dunlop (1945) in an adult receiving too much thiouracil. Davis and Forbes ascribed the effect to the direct action of thiouracil on the fœtal thyroid gland, rather than to lack of maternal thyroxine, for the mother was not myxœdematous. Freiesleben and Kjerulf-Jensen (1947) treated a pregnant patient with methylthiouracil until the fifth month, when the fœtus was removed because the pregnancy was complicated by heart-failure. The fœtal thyroid gland was hyperplastic. Eaton (1945) reported 2 cases in which thiouracil was given during pregnancy. The first patient began with thiourea in the third month, and this was later replaced by thiouracil which was continued until four weeks before term. The baby was healthy. The second patient was receiving thiouracil (600 mg. daily) when she became pregnant, and took this dose throughout the first month and from the third to the fifth months. The dose was reduced to 400 mg. daily for another month, and then to 200 mg. daily until delivery, which was by cæsarean section because of placenta prævia. Three months before delivery the mother's basal metabolic rate was +5%. The baby had an enlarged thyroid gland, but was otherwise normal. The enlargement had subsided after three months, and growth had been normal.

Frisk and Josefsson (1947) described the case of a woman who was taking methylthiouracil (100–200 mg. daily) when she became pregnant. The dose was increased to 200 mg. daily after three months. Treatment was stopped for six and a half weeks, but 300 mg. was given daily for the last seven weeks. The patient never had signs of myxœdema, and the basal metabolic rate was usually +10%, with a minimum of +5%. Uterine myomata necessitated delivery by cæsarean section two weeks before term. The baby was in fairly good general condition, and the thyroid gland was not clinically or radiologically enlarged, but X-ray examination of bones showed retarded development of centres of ossification, the appearance being that of an eight-month fœtus. The serum-cholesterol was 145 mg. per 100 ml. The baby was not breast-fed, and during the first month there was no obvious abnormality in the general condition or behaviour, apart from moderate hypochromic anæmia. In the second month she became agitated and developed exophthalmos. Spontaneous improvement began after two months, and in three months the child seemed normal for her age, apart from the exophthalmos which subsided by the eighth month. The authors' explanation is that thiouracil blocked fœtal synthesis of thyroxine, resulting in increased activity of the hypophysis. Maternal thyroxine prevented myxœdema in the fœtus and suppressed thyrotropic activity, but when the drug was withdrawn, pituitary hyperfunction persisted.

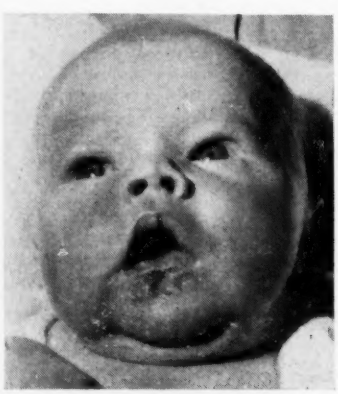
Keynes (1952) described a baby, whose mother received methylthiouracil and sodium thyroxine throughout pregnancy, who, at delivery, had partly obstructed breathing due to a large thyroid swelling which regressed over the next nine days. X-ray examination showed delayed ossification. He also recorded the condition at birth of 19 infants whose mothers had received thiouracil compound during pregnancy. 12 mothers had received the drug for a short time only, and the babies were normal. 6 had received it for a longer period. Premature twins were born to 1 mother. 2 other babies were cretinous with swollen necks; 1 was cretinous without goitre; and 2 had goitres. 1 of the cretinous babies with a goitre was the case described below, and Keynes gives the baby's history in the mother's own words.

No case has been reported of a mother taking thiouracil who breast-fed her baby.

The following case is described because a search of the literature has revealed no other report of an infant, whose mother was treated with thiouracil during pregnancy, who besides having a large thyroid gland, showed clinical signs of hypothyroidism at birth and failed to develop normally.

CASE-RECORD

Mrs. A., aged 29, was first seen in the antenatal clinic on May 2, 1950, when she was four and a half months pregnant. She had 2 normal children, aged 5 and 2. She had severe thyrotoxicosis, the symptoms having begun thirteen months previously. Treatment with methylthiouracil (200 mg. twice daily) was begun on May 25, and was continued throughout pregnancy and the puerperium. At term there was no evidence of thyrotoxicosis apart from exophthalmos. Hydramnios developed, and artificial rupture of the membranes was performed at term on Oct. 5, 1950, fourteen pints of liquor being withdrawn. The baby was delivered spontaneously on Oct. 8 after a labour complicated by uterine inertia. Her colour was good, and she cried at once. Her weight was



The baby on the fourteenth day.

6 lb. 7 oz. She was œdematous all over but no more so than some healthy infants. The anterior and posterior fontanelles were widely open. The eyes appeared widely spaced, and the bridge of the nose was depressed (see figure). The thyroid gland was diffusely enlarged. Breast-feeding was not allowed.

During the next twenty-four hours other abnormalities became apparent. The baby was very lethargic, she cried and moved infrequently, and her muscle tone was poor. There was persistent cyanosis of the extremities, and the skin felt cool. Attempts at sucking were feeble, and feeds were taken very slowly. For the first few days the rectal temperature never rose above 97·2°F, and the pulse-rate varied between 100 and 110 per minute. Apart from further enlargement of the thyroid gland her condition remained stationary for several days, after which she improved in every way.

On the fifteenth day, when she was discharged, she was still lethargic and hypotonic but sucked strongly, and crying was infrequent but lusty. The skin felt warmer, and there was only occasional peripheral cyanosis. The thyroid swelling was subsiding. Rectal temperature was 98°–98·4°F and the pulse-rate 110–120. The serum-cholesterol level was 130 mg. per 100 ml. on the thirteenth day. Although this level was within normal limits, it is not considered to invalidate the diagnosis of hypothyroidism, for there was considerable clinical improvement by the thirteenth day, and in young untreated cretins the serum-cholesterol level may be within normal limits (Bruch and McCune 1944, Topper 1951, Wilkins and Fleischmann 1941).

Owing to domestic difficulties, Mrs. A. failed to keep appointments, and the baby was not seen again until June, 1951, when she was eight months old. She had followed a light with her eyes at two months, and had smiled at four months. She had always been lethargic, and had only recently begun to kick her legs or hold up her head. She was plump and hypotonic, and still had the strange naso-orbital configuration. She smiled and took notice of what was going on, but did not reach out to grasp objects, kicked feebly, and could only lift up her head momentarily. The pulse-rate was 110, and the skin was warm and pink. No thyroid enlargement was detected. No other abnormalities were found, and there was no evidence of hypothyroidism.

Two weeks later a lower central incisor erupted, and at nine months she could kick vigorously, hold up her head, and sit up with slight support, though she could not pull herself up. X-ray examination of the carpus showed centres of ossification for the os magnum and unciform bones on both sides, and diaphyseal dysgenesis was not present.

From Sept. 5 until Oct. 3, 1951, thyroid was given (the dose is unknown), but it was stopped because it was considered to be unnecessary. The mother noticed no change during this period.

Her subsequent progress has been disappointing. The mother reported at seventeen months that the baby was lively and contented, but backward. She could pull herself up into a sitting position, but could not sit or stand without support, and had made no attempt to crawl. She had spoken no intelligible words, and played with toys like a much younger child. She was neither clean nor dry. The anterior fontanelle had almost closed. She had twelve teeth. Her weight was 22 lb., and her height 33 in.

DISCUSSION

Thyroid enlargement in the infant of a mother who received methylthiouracil during pregnancy, and its disappearance after withdrawal of the drug at birth, is to be expected in the light of experimental work (Hughes 1944, Goldsmith et al. 1945, Freiesleben and Kjerulf-Jensen 1946), although few cases have been reported.

The hypothyroidism exhibited by this baby is not difficult to explain. On the thirteenth postpartum day her mother's basal metabolic rate was −5%, and the serum-cholesterol level was raised to 375 mg. per 100 ml. As treatment had been unchanged, she had probably been mildly myxœdematous during the latter part of pregnancy. The fœtus, whose own thyroid function was depressed by thiouracil, must therefore have been receiving insufficient thyroid hormone. After withdrawal of the drug at birth the infant's thyroid gland recovered quickly, and produced enough thyroid hormone to cure the hypothyroidism and prevent its recurrence.

At nine months mental development was retarded, although physical and skeletal development were satisfactory, and there was no evidence of hypothyroidism. Mental retardation may occur in congenitally hypothyroid children in spite of apparently adequate therapy (Aldrich 1936, Bruch and McCune 1944, Lewis 1937, Wilkins and Fleischmann 1941), and Topper (1951) and Bruch and McCune (1944) consider that cerebral damage is the factor which prevents satisfactory mental progress. Lotmar (1929) found histological changes in the brain cells of cretins after death, which he thought to be due to the effect of thyroid deficiency. Tredgold (1929) believed that there were two types of cretin: in one type mental and physical retardation were due to hypothyroidism, and the child became normal under treatment; in the other, the essential condition was primary amentia, the hypothyroidism being a complication, and the child remained mentally defective in spite of treatment.

In the case reported here, it is not possible to tell whether prenatal lack of thyroid is the sole cause of backwardness, or whether primary amentia exists as well. The strange facial appearance, which is unlike that of a cretin or of any named condition, makes the child appear defective. It is not likely that better progress would have been made if thyroid had been given, for recovery from the early hypothyroidism took place spontaneously. There is evidence that thyroid hormone may impair mental capacity when given to cretins in amounts greater than those required for satisfactory physical growth (Bruch and McCune 1944), although Aldrich (1936) advocated giving the largest dose of thyroid tolerated by the patient, in case more thyroid were needed to produce normal mental development than to provide satisfactory physical growth.

This case is reported in order to draw attention to the fact that the administration of thiouracil to a pregnant woman may give rise not only to thyroid hyperplasia, but also to hypothyroidism and permanent damage in the fœtus. The danger could be minimised by careful control of the dosage, so that the mother is not allowed to become myxœdematous. In view of Keynes's report that the babies of mothers who had received the drug for a short time only were healthy, and that 5 out of 7 whose mothers had received it for a longer time were abnormal, it is clearly advisable to give it only for short periods.

SUMMARY

Experimental work on animals has shown that the administration of thiourea or its derivatives to pregnant animals may lead to thyroid hyperplasia and cretinism in the young animal.

Only 10 cases of abnormality ascribed to thiouracil in the human fœtus or newborn infant have been reported. These are described.

A baby girl, whose mother received thiouracil during pregnancy, had hypothyroidism at birth. She recovered spontaneously, but her mental development was subsequently retarded.

The cause of the hypothyroidism and mental retardation is discussed.

I wish to thank Dr. Simon Yudkin for his help and encouragement in the preparation of this paper.

REFERENCES

Aldrich, C. A. (1936) *J. Pediat.* **8**, 381.
Astwood, E. B. (1943) *J. Amer. med. Ass.* **122**, 78.
— Vander Laan, W. P. (1946) *Ann. intern. Med.* **25**, 813.
Bain, L. (1947) *Sth. med. J., Nashville*, **40**, 1020.
Bell, G. O. (1950) *J. Amer. med. Ass.* **144**, 1243.
Bruch, H., McCune, D. J. (1944) *Amer. J. Dis. Child.* **67**, 205.
Caren, R. (1949) *J. clin. Endocrin.* **9**, 903.
Carns, M. L., Poser, R. F. (1946) *Wis. med. J.* **45**, 205.
Davis, L. J., Forbes, W. (1945) *Lancet*, ii, 740.

References continued overleaf

TRANSIENT HYPOTHYROIDISM IN A NEWBORN INFANT

DAVID MORRIS
M.R.C.P., D.C.H.
PÆDIATRICIAN, THE BRITISH HOSPITAL FOR MOTHERS AND BABIES, WOOLWICH

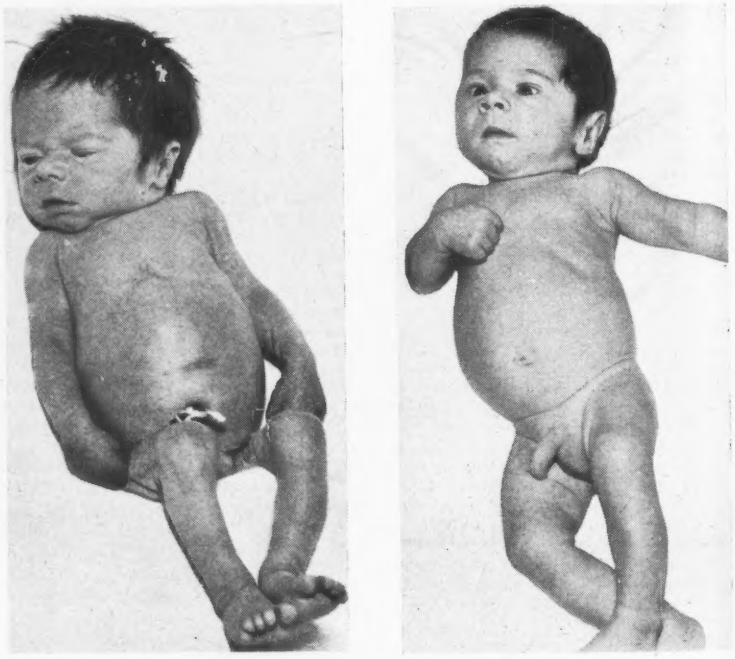
SINCE the advent of thiourea and thiouracil, thyrotoxicosis during pregnancy is being treated by these drugs with increasing frequency. There have been many reports of the success of this treatment with no apparent harmful effect on the newborn infants. Others, however, have shown that the fœtus may be affected. Davis and Forbes (1945) reported the sudden death from unknown cause of a pregnant woman who had been taking thiouracil before and during her pregnancy; the thyroid gland at the fœtus was hyperplastic and hypertrophied. Freiesleben and Kjerulf-Jensen (1946) found a hyperplastic thyroid gland in a fœtus of a woman who had been treated with methylthiouracil for five months and whose pregnancy was terminated because of heart-failure. The literature has recently been well reviewed by Elphinstone (1953) who described clinical signs of hypothyroidism at birth in an infant whose mother had been treated with thiouracil during pregnancy. The following is a report of a further case.

CASE-RECORD

Mrs. H., a primipara aged 20, first attended the antenatal clinic when she was about fourteen weeks pregnant. Her past history had been uneventful until she had been pregnant one month, when she had palpitations, sweating, and slight nervousness. She was seen by a physician who suspected that these symptoms might be due to thyrotoxicosis, and she was admitted to hospital for further observation and investigation. The diagnosis of thyrotoxicosis was confirmed. Her basal metabolic rate was + 21%, and serum-cholesterol 142 mg. per 100 ml. Bed rest and phenobarbitone (gr. $^1/_2$ t.d.s.) were tried, but she failed to improve, and she was given methylthiouracil (100 mg. b.d.) in addition to the phenobarbitone. This treatment was continued throughout her pregnancy, which was otherwise normal, and she went into labour at term.

She gave birth without difficulty to a small male infant weighing 5 lb. 4 oz. Respirations were established immediately after birth, and nothing unusual was noted until ten minutes later when the infant became limp and collapsed; the rectal temperature was 95°F. He was placed in an incubator, and during the next twelve hours his condition slowly improved and his temperature returned to normal. During the next three days his appearance and behaviour caused comment, for he was very inactive and reluctant to suck, and he looked "odd."

I first saw him on the third day of his life when the appearance (fig. *a*), the inactivity, the cold dry skin, the pulse-rate of 120 per minute, and a palpable thyroid gland suggested a diagnosis of hypothyroidism, especially in view of the administration of thiouracil during pregnancy. The serum-cholesterol was 312 mg. per 100 ml. and the electrocardiogram showed low voltage in the three standard leads. X-ray examination showed no ossification centre at the lower end of the femur. As the infant's condition was deteriorating, thyroid (gr. $^1/_3$ b.d.), was given by mouth for ten days with remarkable clinical improvement. The pulse-rate rose to 170, he sucked well, became active, and regained his birth weight by the fourteenth day of life. No further thyroid was given and satisfactory progress was maintained.



a *b*

The baby (*a*) at birth and (*b*) at eight weeks.

He was discharged when eight weeks old, weighing 7 lb. and taking normal feeds of dried milk (breast-feeding had never been established). The serum-cholesterol was then 188 mg. per 100 ml., the electrocardiogram showed an increased voltage, his appearance was that of a normal child (fig. *b*), and the enlargement of the thyroid gland had subsided. When seen one month later he appeared and behaved normally.

He recently attended for review when eight months old. The parents had noted nothing unusual about him although his head was obviously large, the circumference being 20 in. He was admitted for further investigation; a ventricular tap produced a normal fluid under increased pressure, and, on X-ray examination, the skull was reported to be large with a thin vault due to hydrocephaly with no indication of the cause. He was seen by a neurosurgeon who thought there was probably a stenosis of the aqueduct or an Arnold-Chiari malformation and that no surgical treatment was advisable. There were no clinical signs of hypothyroidism,

DR. ELPHINSTONE: REFERENCES—*continued*

Donald, J. B., Dunlop, D. M. (1945) *Brit. med. J.* i, 117.
Eaton, J. C. (1945) *Lancet*, i, 171.
Eisenberg, L. (1950) *N.Y. St. J. Med.* **50**, 1618.
Freiesleben, E., Kjerulf-Jensen, K. (1946) *Nord med.* **32**, 2811.
— — (1947) *J. clin. Endocrin.* **7**, 47.
Frisk, A. R., Josefsson, E. (1947) *Acta med. scand.* suppl. no. 196, p. 85.
Goldsmith, E. D., Gordon, A. S., Charipper, H. A. (1945) *Amer. J. Obstet. Gynec.* **49**, 197.
Hughes, A. M. (1944) *Endocrinology*, **34**, 69.
Keynes, G. (1952) *J. Obstet. Gynæc.* **59**, 173.
Lahey, F. H., Bartels, E. C. (1947) *Ann. Surg.* **125**, 572.
Lewis, A. (1937) *Lancet*, i, 1505; *Ibid*, ii, 5.
Lotmar, F. (1929) *Z. ges. Neurol. Psychiat.* **119**, 491.
Mussey, R. D., Haines, S. F., Ward, E. (1948) *Amer. J. Obstet. Gynec.* **55**, 609.
Palmer, M. V. (1945) *Ann. intern. Med.* **22**, 335.
Reveno, W. S. (1948) *J. clin. Endocrin.* **8**, 866.
Rose, E., McConnell, J. (1944) *Amer. J. med. Sci.* **208**, 561.
Sexton, D. L. (1946) *Sth. med. J., Nashville*, **39**, 891.
Topper, A. (1951) *Amer. J. Dis. Child.* **81**, 233.
Tredgold, A. F. (1929) Mental Deficiency. 5th ed. London; p. 274.
Trotter, W. R. (1951) Personal communication.
Vogt, E. (1946) *Nord. med.* **31**, 1733.
Whitelaw, M. J. (1947) *J. clin. Endocrin.* **7**, 767.
Wilkins, L., Fleischmann, W. (1941) *J. Amer. med. Ass.* **116**, 2459.
Williams, R. H. (1946) *J. clin. Endocrin.* **6**, 1.
— Kay, G. A., Jandorf, B. J. (1944) *J. clin. Invest.* **23**, 613.

and the thyroid function assessed by radioactive iodine uptake was normal. The serum-cholesterol was 160 mg. per 100 ml. on three occasions. A radiograph of the wrist showed no carpal bones.

He is retarded in his development, and although it is difficult to be certain, it seems probable that this is due, not to hypothyroidism, but to the hydrocephalus which is most likely coincidental.

CONCLUSION

Although thyrotoxicosis during pregnancy can usually be effectively and safely treated with thiouracil, this report and that of Elphinstone (1953) shows that the procedure is not without risk. As thiouracil is excreted in the milk (Williams et al. 1944), the baby should not be breast-fed. It is suggested that the smallest possible dose for clinical control be used when thiouracil is given in the treatment of thyrotoxicosis during pregnancy, and that, if possible, the dose should be reduced in the last month of pregnancy or omitted altogether, as advocated by Clayton and Oram (1951).

SUMMARY

A male infant, born at term to a mother who had received thiouracil for thyrotoxicosis during most of her pregnancy, showed clinical signs at birth of hypothyroidism, with an enlarged thyroid gland. After a few days' treatment with thyroid extract he became and remained normal without further thyroid. There was no demonstrable evidence of hypothyroidism at eight months of age, but hydrocephalus had developed which was thought to be coincidental.

I am indebted to Dr. S. Karani for allowing me access to his notes; to Mr. G. C. Knight for his neurosurgical opinion; and to Dr. A. Stuart Mason for carrying out the radio-iodine investigation.

REFERENCES

Clayton, S. G., Oram, S. (1951) Medical Disorders during Pregnancy. London.
Davis, J. L., Forbes, W. (1945) *Lancet*, ii, 740.
Elphinstone, N. (1953) *Ibid*, i, 1281.
Freiesleben, E., Kjerulf-Jensen, K. (1946) *Nord. med.* **32**, 2811.
Williams, R. H., Kay, G. A., Jandorf, B. J. (1944) *J. clin. Invest.* **23**, 613.

THE RADIO-ELECTROPHYSIOLOGOGRAM

RADIO TRANSMISSION OF ELECTROPHYSIOLOGICAL DATA FROM THE AMBULANT AND ACTIVE PATIENT

CYRIL STANSFELD PARKER
M.D. Manc., D.P.M.
CONSULTANT PSYCHIATRIST, PRESTON, BLACKPOOL, AND WHITTINGHAM HOSPITAL GROUPS

CHARLES C. BREAKELL
L.D.S. Manc., A.M.Brit.I.R.E.
HON. CONSULTANT ENGINEER, ELECTRO-ENCEPHALOGRAPHY DEPARTMENT, WHITTINGHAM HOSPITAL

F. CHRISTOPHERSON
TECHNICIAN-IN-CHARGE, ELECTRO-ENCEPHALOGRAPHY DEPARTMENT, WHITTINGHAM HOSPITAL

THE successful radio transmission of electro-encephalograms (E.E.G.) and electrocardiograms (E.C.G.) has already been reported (Breakell and Parker 1949, Breakell et al. 1949). Here we describe a radio transmitter carried by the subject and modulated by his E.E.G. or E.C.G. The subject is thus completely mobile and free from restraining leads, and may perform any special tasks or go about normal activities while his E.E.G. or E.C.G. is radio-transmitted to a receiver, which records it in one of the conventional forms.

Applications

E.C.G.

In its present form the apparatus is ideal for the routine clinical application of the two-step cardiogram exercise tests of Master and Oppenheimer (1929; see also Master 1935), because an instantaneous record is obtained on cessation of the exercise and to a considerable extent during the exercise (fig. 1). No doubt cardiologists could devise similar tests of broader scope using this apparatus in view of its much greater mobility and the freedom of restraint in the patient's activities.

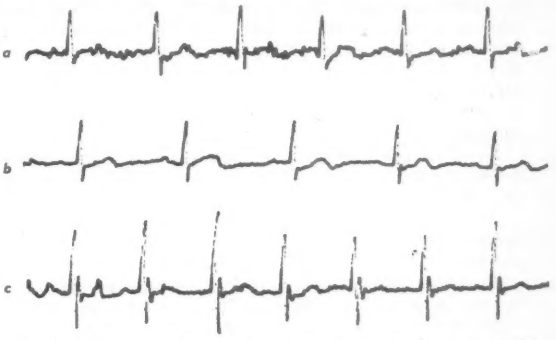


Fig. 1—E.C.G.: *a*, patient marking time; *b*, patient walking normally; *c*, patient walking upstairs.

The factor that at present limits the patient's movements is the electrostatic condition of the atmosphere. When there is little static—e.g., on wet days—much more vigorous activity can be associated with clear recording of the cardiogram. The same effect can be obtained by damping the atmosphere of a room or by using a trailing earth. On many days the cardiogram can be followed during normal walking without special precautions (fig. 1*b*). (This problem of static artefact is under active research, and there is reason to believe it may yield to special methods.)

It is possible with the apparatus to take continuous E.C.G. recordings of a mobile subject for several hours during which frequent samples of the E.C.G. are obtained in the periods of quieter activity. Alternatively, the subject may be asked to perform special tests, such as ladder-climbing, or be submitted to situations producing anxiety or other stress.

Fig. 1 illustrates E.C.G. recorded under various conditions. The instrument is electronic, and there is, of course, none of the familiar fuzz of the ordinary E.C.G. base-line.

E.E.G.

The problem of static is more troublesome with E.E.G. than with E.C.G., owing to the higher gain required, especially as static artefacts *appear* as low-frequency swings in the record. This makes the recording of lower E.E.G. frequencies difficult when the subject is actively moving about. By using analyser filters in the receiver however, the higher E.E.G. frequencies can be studied under conditions of the most vigorous activity. The filters are specially designed to reduce "ringing" as much as possible. Analyser filters have their own particular difficulties but can be used satisfactorily for certain types of information. There is little limit to the patient's mobility with this method; he can move more or less where he will.

In particular we are beginning to apply this study of higher frequencies to the prefrontal areas, with especial reference to anxiety-provoking situations such as

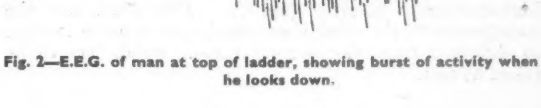


Fig. 2—E.E.G. of man at top of ladder, showing burst of activity when he looks down.

(1) ladder-climbing (figs. 2 and 3); (2) holding leads from a fearsome-looking X-ray switch panel with suggestion of increasing current as switches are pressed and knobs turned, although no current is passed at all (fig. 4); (3) locked up in a small dark room; (4) making a public speech; (5) balancing at a height; and (6) fire-extinguishing drill (fig. 5).

Muscle-action potential can also produce a β frequency in the E.E.G., but this artefact is excluded by voluntary test movements before the exercises:

(1) Failure to produce β by voluntary muscular effort. Frowning, looking surprised, head-turning, teeth-clenching, arm-raising, walking, arm-straining, leg-raising, leg-straining.

(2) Where possible, repetition of the test in absence of anxiety without occurrence of β. For example, ladder-climbing may be done repeatedly without production of β, and then show β when situations are altered to produce anxiety on climbing.

(3) Absence of β during similar active movement when there is absence of β-productive situation—i.e., a quiet base-line except during the anxiety situation.

β frequency is the term applied to rhythm at 14–25 cycles per sec. It is especially seen in the frontal areas and is thought in some cases to be associated with anxiety. For example, it was noticed in one exercise that in four different men β rhythm occurred when they reached the middle of an extension ladder (fig. 6). This *appeared* on inspection to be associated with either increased sway in the middle of the ladder or a rope knot at this point requiring careful negotiation. No conclusions are intended from this particular illustration, but one may speculate whether the instrument could be used in this way to indicate the points of irritation or special attention in performance of a given task—e.g., routine factory job—and perhaps lead to elimination of points of difficulty in the job performance, or as objective evidence of acquisition of confidence during learning of a particular act. Perhaps we have a machine here which will give us objective evidence of anxiety as opposed to subjective.

Fig. 3—Man climbing ladder while wearing apparatus for recording E.C.G. and E.E.G.

A further point which has arisen in our initial tests is that the prefrontal cortex is relatively quiescent for considerable periods during continuous recording. For example, in one subject there was no great activity throughout a game of deck tennis and "shooting in" at football, whereas in the same subject β activity is easily provoked by anxiety situations of a particular kind. It also seems from our initial tests that different people exhibit β in anxiety situations peculiar to themselves—e.g., climbing a ladder might never produce β in one person but being shut up in a dark room would. In one test a fireman got stuck on the underside of a ladder at roof height when the apparatus caught in the ladder rungs. This gave him "a very nasty few moments" and was reflected in the E.E.G. as a prolonged burst of high-voltage β activity (fig. 7). This illustrates the spontaneity of the situations which may arise in testing, so different from the normal E.E.G., which has to be taken at rest.

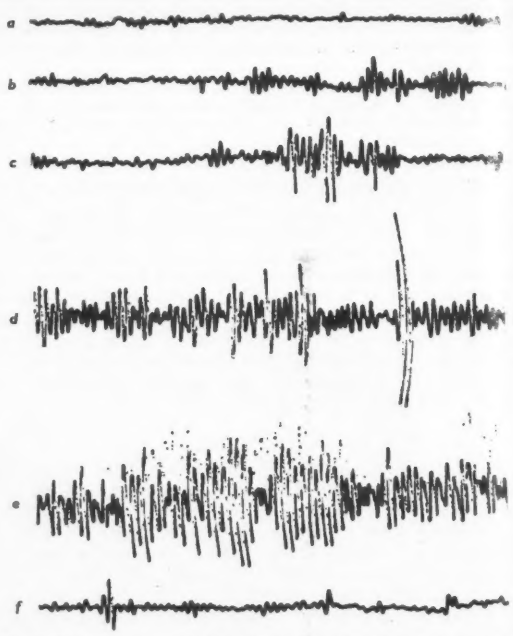


Fig. 4—E.E.G. of person, holding leads from electric switch panel, who has been told that he will feel increased current when switches are pressed and knobs turned, although no current is passed at all: *a*, before test; *b*, while test is being explained; *c*, while knobs are being turned; *d*, when big switch is pressed; *e*, when "full power" has supposedly been turned on; *f*, after test. Note increasing β activity while switch panel is being manipulated.

One of the probable reasons why the E.E.G. has been of less immediate clinical application in psychiatry than might have been thought is that recording has hitherto had to be done with the subject at rest. This portable apparatus now enables us to study the E.E.G. in everyday situations.

Fig. 8 compares an ordinary direct E.E.G. recorded simultaneously with a radio E.E.G.

The Apparatus

The design of a suitable radio transmitter presented many difficulties, the main requirements being economical operation to restrict weight of batteries or other power supply, small size, and an almost infinite capacity to withstand rough usage during the tests (fig. 9).

Fig. 5—Fireman wearing apparatus and using fire-extinguisher.

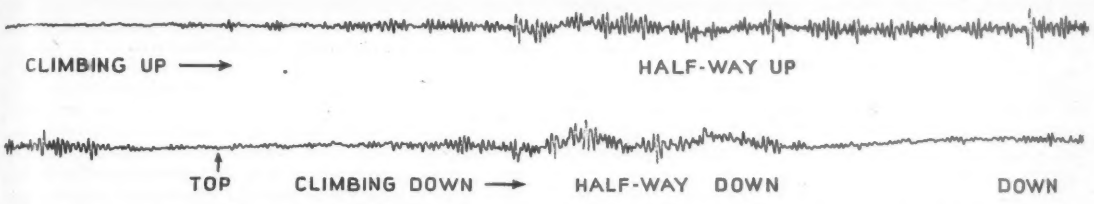


Fig. 6—E.E.G. of man climbing up ladder and down again ; note β activity when he is half-way up and again when he is half-way down.

It was anticipated that, during exercise, the patient's movements would cause variation in the strength of the signal, owing to changes in the standing wave pattern and to reflections from nearby buildings, lamp-posts, drain pipes, and other metalwork in the vicinity.

Since the wave-length allocated is just below two metres (158·75 megacycles per sec.), the probability was that such variations would occur at frequencies falling within the low-frequency band required for electro-

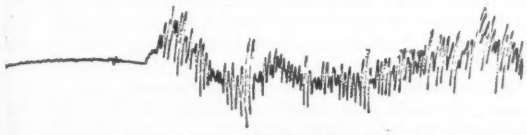


Fig. 7—E.E.G. of man climbing ladder who accidentally slipped off rungs and swung from underside of ladder, showing burst of β activity.

encephalography and interfere with the record. Tests proved such fears to be well-founded.

It was apparent that, if amplitude modulation were applied to the carrier wave, some form of automatic volume control would also be required at the receiving, end ; and, as a quick response would be necessary, the time constants of such a device would be short enough to permit distortion of lower E.E.G. frequencies. But Canadian workers seem to have attempted amplitude modulation (Glasscock and Holter 1949), though later they used frequency modulation (Glasscock and Holter 1952).

Full consideration of alternative methods appeared to indicate that the use of frequency modulation (F.M.) would offer the greatest chance of success since, owing to limiter action and other reasons a F.M. receiver is relatively insensitive to amplitude variations, at least within certain limits.

For preliminary tests a small F.M. transmitter was built. Seven valves, of indirectly heated subminiature

Fig. 8—Simultaneous records of E.E.G. from same electrodes in a child aged 12 years : *a*, radio ; *b*, direct.

type, were used in a circuit embodying master oscillator and frequency-multiplying stages with integral head-amplifier and reactor stages.

The apparatus was fitted in a light copper box measuring $6 \times 3^1/_2 \times 3^1/_2$ in. and, although it was fairly successful in use, operation was rather difficult owing to frequency drift caused by temperature rise. This produced a change in the recording base-line necessitating frequent retuning of the receiver.

Further tests indicated that if the instrument was to be of clinical value, the use of a free-running oscillator could not be justified, and that apparatus built for permanent use would have to be crystal-controlled. This would ensure a steady basic frequency and permit the use of a crystal-controlled receiver, thus eliminating all tuning adjustments during operation, allowing undivided attention to recording.

The use of crystal control is not without difficulty, since phase modulation is also implied, leading to a loss of gain equal to 6 db. per octave as the frequency of the modulating source is reduced ; hence, at frequencies common in E.E.G. work, an inordinate amount of amplification would be required, together with the use of an amplifier having a rising characteristic with reducing frequency.

The apparatus in use at present was designed to overcome the difficulties described and has proved to be satisfactory in service.

Construction was undertaken in two stages. A conventional crystal-controlled transmitter, with phase modulation, was built on one chassis, this being bolted to a second and similar chassis carrying the head amplifier and an oscillator capable of reasonably pure output at a frequency of 5 kc. per sec.

Fig. 9—Apparatus in position.

After amplification the E.E.G. wave-form is applied to the suppressor grid of the 5 kc. oscillator producing an amplitude-modulated tone, which is then coupled, via a suitable transformer, to the control grids of the phase modulator valves.

With the head electrodes short-circuited the carrier wave will be deviated to a predetermined degree at the rate of 5 kc. per sec. The arrival of an E.E.G. signal then causes a change in the extent to which the carrier wave is deviated.

At the receiver the signal is reproduced as a 5 kc. tone with the E.E.G. wave-form superimposed thereon, and it is a simple matter to demodulate this, to remove the 5 kc. component, and to restore the E.E.G. to a form suitable for amplification to the desired level for recording.

It will be obvious that, by the addition of other tone generators operating at suitable frequencies, each connected to its own amplifier, a number of channels could be accommodated for the simultaneous transmission of other physiological data—pulse-rate, electrocardiogram, &c.—the information being extracted at the receiver by passing the output through filter units.

As the transmitter was built for test purposes, no attempt was made to achieve minimum size ; and, as ordinary valves were used in most of the stages, power-supply requirements are rather heavy. Fortunately a new light-weight accumulator of the silver-zinc type is now generally available enabling a small rotary convertor

to be used for high-tension supply, providing a useful recording time of about four hours.

Conclusions

We are concerned in this article merely with describing the apparatus and its possible applications, and the tests mentioned are not intended to indicate any conclusions but simply mode of use of the apparatus and possible lines of research with it.

The E.E.G. and E.C.G. have so far been mentioned; but, of course, any physiological phenomenon which can be expressed electrically could be studied in the same way with this apparatus—e.g., radio tracer work; muscle-action potentials; and electrical activity of mucosa. No doubt other workers will see applications to their own especial field.

There are many uses for this apparatus. For example, the phonocardiogram could probably be studied in this way, giving records of the heart sounds during everyday and unrestricted activity. Again, the apparatus might be usefully adapted to animal experiments where freedom of movement in the animal is desired.

Our thanks are due to Dr. A. R. Grant, medical superintendent, Whittingham Hospital, for his most helpful encouragement.

REFERENCES

Breakell, C. C., Parker, C. S. (1949) *Lancet*, i, 167.
— — Christopherson, F. (1949) *Electroenceph. clin. Neurophysiol.* **1**, 243.
Glasscock, W. R., Holter, N. J. (1949) *Rocky Mtn med. J.* **46**, 748.
— — (1952) *Electronics*, **25**, 126.
Master, A. M. (1935) *Amer. Heart J.* **10**, 495.
— Oppenheimer, E. T. (1929) *Amer. J. med. Sci.* **177**, 223.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Medical Problems in Korea

THE United Services section of the society met on June 10, with Sir Stanford Cade, the president, in the chair.

Lieut.-Colonel R. L. MARKS described the medical picture in Korea as he had seen it from January, 1952, to January, 1953, when he was commanding a field ambulance in the Commonwealth Division. At this time the division held a static position and there was constant patrolling, shelling, and occasional attacks by both sides. Enemy air activity was virtually nil and this had influenced forward medical arrangements, particularly evacuation by helicopter. There had been a steady trickle of casualties, with some increase after an attack—the greatest number at any one time was 76. The terrain consisted of small hills, scrub, ploughed fields, and paddy fields; the earth roads were dusty in the summer and a sea of mud after rain. The front-line was reached by travelling in a jeep to company level, and then walking forward in gradually deepening trenches which eventually were about eight feet deep. Off these were a number of two to four man dugouts, lit by candles and heated by stoves, in which the men lived.

The R.M.O. was situated near battalion headquarters. Five miles back was a field ambulance which had two casualty-clearing posts, two miles behind the front-line. A field dressing station of 120 beds, with a surgical team and psychiatrist, was ten miles farther back, and on one flank an American M.A.S.H. (mobile army surgical hospital), the main centre for surgery, was situated. From the M.A.S.H. cases were evacuated by train to Seoul, and, if necessary, Commonwealth casualties went by air from Seoul to Kure in Japan and the Americans to Tokyo. Cases not likely to recover within three weeks were not kept in Korea. The advanced dressing station held cases for up to seven days, and a reserve field ambulance of 100 beds held cases likely to recover within three weeks. Because of the static nature of the war and the absence of enemy air activity, the policy was to hold the sick as far forward as possible.

With the help of a helicopter, a casualty could be in the hands of the surgeon forty-five minutes after reaching the R.M.O. Some revision of the policy on morphine administration was therefore necessary to prevent cases arriving at the M.A.S.H. too heavily drugged. Only the R.M.O. gave morphine; and he also gave penicillin and set up dextran drips when needed. Medical conditions were mostly seasonal: in the winter there were colds, influenza, and a very few cases of frostbite; in summer the main cause of disability was skin diseases and, to a lesser extent, malaria and intestinal infections. From May until November there were sporadic cases of hæmorrhagic fever. The incidence of gonorrhœa and chancroid was appreciable, and there was some non-specific urethritis, but no syphilis. Initial diagnosis and treatment (lasting two days) of venereal diseases was carried out at the advanced dressing station, and continuation treatment by the R.M.O. There were few psychiatric casualties. Road accidents and burns from stoves accounted for the considerable number of accidental injuries.

Major F. J. INGHAM, introducing the subject of Army health, said that in Korea malaria was endemic, intestinal diseases and tuberculosis were common, and typhus and relapsing fever occurred. On the whole, the health of the Army had been good.

The climate was extreme, and temperatures lower than 11°F and as high as 95°F were encountered. For the winter, special clothing had been provided, including a string vest, combat jacket and trousers, a lined parka coat, special boots, and three pairs of gloves. Slacks, a flannel shirt, and ammunition boots were worn in summer. The ration per day was 5100 calories in winter and 4500 in summer. Water was available at three fixed water-points in the divisional area. In some areas a tributary of the Imjin river was used. The bunkers in which the front-line troops lived were infested with rodents which were a menace to the troops. 'Warfarin' was successful in controlling the rodents, and D.D.T. powder dealt with the lice. D.B.P. and D.M.P. were used as insect repellents. Korea was a fairly large reservoir of *Plasmodium vivax*, but the incidence of malaria in the U.N. Forces was kept low by suppressive proguanil ('Paludrine') (100 mg. daily). Civilians were given mepacrine. In the Commonwealth division there had been 94 cases of hæmorrhagic fever, with 3 deaths. Infection was localised to the forward areas, especially rat-infested or swampy regions. To protect against the vectors of the disease clothing was impregnated with D.B.P. and antirodent measures were carried out. There were not many flies in the forward areas and very few clinical cases of dysentery.

Major-General A. G. HARSANT spoke of the development of the Commonwealth Division in Korea. American Headquarters were at Tokyo, where they had their main hospital. The Commonwealth hospital was at Kure, where there were 1000 beds. The director of medical services for Korea and the consultants in medicine and surgery (all of whom are American) were at Seoul.

At the M.A.S.H. primary surgery was carried out on battle casualties, who were then evacuated by air or train to Seoul where secondary suture might be carried out. Men not retained in Korea were flown from Seoul to Iwakuni by R.A.A.F. Dakotas, and thence by train or launch to Kure; or, if they needed special surgical treatment, they were flown direct to the American hospital in Tokyo, where there were specialist surgical teams—e.g., maxillofacial, thoracic, and neurosurgical teams. All neurosurgical cases were treated by the Americans, who had two neurosurgical teams at M.A.S.H.s in Korea and a base unit in Tokyo, and casualties from the whole front were flown by helicopter to one or other of these.

General Harsant observed, that with the present static conditions, air superiority, and freely available helicopter evacuation, casualties could reach the surgeon within an hour or two. With such rapid evacuation of casualties, the R.M.O. could become responsible for initiating resuscitation, and he could give transfusions of dextran, for example, before the case was evacuated by helicopter. Dextran was used in preference to plasma, which carried a risk of hepatitis. Blood was collected from local sources by a field-transfusion team for the Commonwealth hospital in Japan, but blood in Korea was freely available from American sources: this was for the great part flown from the United States.

The body armour that was in use gave efficient protection to the chest and abdomen. Its main drawback was its weight. Cases of traumatic anuria were sent to a special American research unit in Korea where there was an artificial kidney. The Americans were very keen that research should be carried out as far forward as possible, and they had a research team at some of the M.A.S.H.s. In total war they visualised having a forward research hospital. The functions of these teams were to try to solve the problem of the last 1–2% mortality, to provide teaching facilities, and to act as a testing-ground for new ideas.

Lieut.-Colonel K. P. BROWN described the hæmorrhagic fever first encountered by the U.N. Forces in the spring of 1951. It had previously appeared among Japanese and Russians. There had been a further outbreak in the autumn of 1951, and in all about 1000 cases, mostly American. A special M.A.S.H. was now dealing with all cases. Only about 60 Commonwealth troops had been infected. The Japanese view was that the disease was due to a virus, but it was now thought to be caused by a rickettsial-like body. The disease was carried by mites and was commonest in scrub and marshy areas. The incubation period was two to three weeks. The disease was characterised by increased permeability and dilatation of the capillaries and by kidney damage. The increased capillary permeability sometimes led to œdema, often in the retroperitoneal region. The onset was acute, often with severe headache and chills, and a temperature of 103°. There might be severe backache which was very difficult to relieve. Considerable thirst was a feature of the early stages, and it had been found that giving too much fluid at this stage increased the tendency to vomit. Petechial hæmorrhages began to appear about the third day. After this, injections and handling of the patients were liable in severe cases to cause echymoses. Early diagnosis and treatment appeared to have reduced the liability to severe hæmorrhage later. The fever lasted three to five days, ending with rapid lysis. Some hypotension usually followed, and sometimes there was severe shock and hæmorrhage. All patients had some kidney damage, and albuminuria appeared about the third day. Oliguria, which could go on to anuria, followed the febrile stage, but it was not related to the hypotension. About the sixth day there was a diuresis that could be so rapid as to require replacement therapy. The specific gravity of the urine, high in the early stages, fell to 1010 in the oliguric phase and to 1002–1004 during the diuresis. After about three months the patient was usually able to concentrate urine to about 1025. The white-cell count was low in the early stages but began to rise about the third day, with a slight shift to the left. The platelet-count fell by the third or fourth day, and there was a definite increase in the capillary fragility. Sometimes there was a characteristic dilatation of the capillaries of the face and sclera, giving a clue to the diagnosis, which was otherwise difficult. The mortality-rate was about 5%. There was no specific therapy and convalescent serum had been useless in treatment.

Suspected cases of hæmorrhagic fever were evacuated. Patients with this disease travelled badly and it was the custom to give strong sedatives before evacuation by helicopter. Sedation was continued throughout the early stages of the disease. Fluid intake was kept on the low side in the early stages, for too much fluid could produce œdema later. The artificial kidney, which had been used in anuria and azotæmia, had not been successful in hæmorrhagic fever, but it had been a great help in traumatic anuria. Commenting on the similarity between hæmorrhagic fever and scrub typhus, Lieut.-Colonel Brown said that it was odd that hæmorrhagic fever should be prevalent in Korea when there had been only 2 cases of scrub typhus.

Malaria had not been a great problem, and had been treated with quinine and pamaquin. Infective hepatitis was the greatest waster of man-power and there were very large numbers of cases. Nothing new had appeared in the treatment. All U.N. troops were protected against Japanese-B encephalitis in 1951 but not thereafter. There had been only 2 Commonwealth cases. Seoul was the centre of an area where paragonimiasis occurred. This was a lung-fluke infection, the X-ray appearance of which was similar to that of tuberculosis; but there had been no cases in U.N. troops.

Lieut.-General Sir FREDERICK HARRIS, director-general, Army Medical Services, said that this campaign was unique in many respects—the absolutely static nature of the war, the complete air superiority of the U.N. Forces, and the wonderful way in which some twenty nations were working together in complete harmony. This coöperation was, he thought, a remarkable achievement and one which would prove to be a great contribution to the peace of the world.

Reviews of Books

The Nature of Virus Multiplication

The Second Symposium of the Society for General Microbiology. Editors: Sir PAUL FILDES, F.R.S., and W. E. VAN HEYNINGEN. London: Cambridge University Press. 1953. Pp. 320. 35*s*.

OPINION about recording the proceedings of congresses and symposia is evenly divided. Some would like verbatim records of every word spoken or implied, while others would be content to let the hot air drift upwards to the stratosphere and the sound waves to fade gently into the distance. The Society for General Microbiology has sensibly compromised in its account of the society's second symposium on the nature of virus multiplication. Sir Paul Fildes and Dr. van Heyningen are to be congratulated on having edited this "idealised" version of the proceedings, in which the contributors to the discussion were given an opportunity to polish and paraphrase their questions and answers before these appeared in print. Those who were present at the symposium may have some difficulty in recognising some of the contributions, but they will still be able to follow with entertainment and interest the Lwoff-Boyd controversy on prophage, the Fulton-Hoyle dispute on influenza-virus growth, and a host of Bawden-Pirie-isms on every conceivable aspect of virus multiplication. This symposium brought together workers with widely different interests and viewpoints, and the discussions covered protein synthesis in general as well as the growth of plant, animal, bacterial, and insect viruses. This book is therefore more than a record of the proceedings; it is a valuable textbook for those who require to know something of the general aspects of viruses and of their points of similarity and difference.

The Pharynx

ABRAHAM R. HOLLENDER, M.D., F.A.C.S., emeritus professor of otolaryngology, University of Illinois College of Medicine. Chicago: Year Book Publishers. London: Interscience Publishers. 1953. Pp. 550. 110*s*.

THIS new work "dealing with direct and related problems concerning the pharynx" seems to have been produced mainly because of the editor's "own special interest in the various aspects of this important organ,"

and it cannot be said to contain anything new. Anatomy and physiology are well described, and there are some unusually good chapters—on the blood dyscrasias, on choanal atresia, and on abscesses of the pharynx. The problems of tonsillectomy and poliomyelitis, focal sepsis, and tonsillectomy in the allergic child are discussed wisely and at some length. But, though carcinoma of the hypopharynx must surely be regarded as truly "pharyngeal"—in its site of origin, its natural history, its behaviour, and its management—this highly important subject is dismissed in but a few words in a chapter on pathology. Printing and production are excellent.

Die körperlichen Behandlungsverfahren in der Psychiatrie

Ein Lehr-und Handbuch. Vol. I. Die Insulinbehandlung. Dr. MAX MÜLLER, a.o. Professor für Psychiatrie an der Universität Bern. Stuttgart: Thieme. 1952. Pp. 295. DM. 36.

Prof. Max Müller, of Berne University, was one of the first to see the spark of genius and the novelty in Sakel's "insulin treatment" of psychoses, which shared the appearance of "foolishness" characteristic (in the words of A. N. Whitehead) of all really new ideas. Müller applied the hypoglycæmic treatment in schizophrenia as early as 1935, and his well-equipped department at Münsingen Mental Hospital was to become a model of organisation and a centre of teaching for psychiatrists from all over the world. Among his extensive writings on this and other treatments, the present manual of nearly 300 pages deals with insulin treatment only.

He attempts to cover the remarkable overgrowth of literature in this field in all languages, reviewing the varied publications critically, although in places not critically enough. Of the 70 pages on physiology, pathology, and psychopathology, a good deal refers to work by clinicians without much insight into the physiological and pathological problems, and interests neither the expert nor the physician practising the treatment. Similarly, some obsolete oddities could be usefully weeded out of the chapters on technique and its modifications and complications. The section on indications, results, and theories is concise, and clearly shows the many debatable points in the mode of operation of the hypoglycæmic treatment and the difficulty in judging its efficacy.

The great value of the book lies in its detached and objective attitude, based on an extensive practical experience and on a strong desire to help patients suffering from one of the most serious psychiatric diseases.

African Highway

The Battle for Health in Central Africa. Sir MALCOLM WATSON, M.D., LL.D., F.R.F.P.S., honorary consultant, Ross Institute of Tropical Hygiene. London: John Murray. 1953. Pp. 294. 63*s*.

IN 1929 the Rhodesian copper mines appointed Sir Malcolm Watson and other members of the staff of the Ross Institute as medical advisers. This book sets out to explain how, in a quarter of a century, an unhygienic tropical rural area has been converted into a healthy and flourishing industrial mining district. Sir Malcolm is clearly a great believer in the benefits which private enterprise, with sound medical advice, can confer on both European employers and native labour in the tropics, and he is highly suspicious of government schemes. In the present uncertainty about the future political development of Central Africa, his great experience of health problems should be invaluable. Unfortunately, however, his book is too largely composed of extracts from reports of malariologists, personnel managers, chief medical officers, and field engineers, of financial statements of copper mines, and of detailed instructions for buildin , for example, an African hospital and a smoking-pit latrine. Much of the material is not recent, and though every reader, whether he has a wide knowledge of tropical life or has never left England, will find many bits and pieces of great interest, the work as a whole lacks continuity of presentation and style, and thus makes difficult reading. The 79 excellent and well-chosen photographs are a more vivid testimony to the achievements recorded.

Cortisone et corticostimuline (A.C.T.H.) en rhumatologie

F. COSTE, professeur de Clinique Rhumatologique; J. CAYLA, chef de Clinique Rhumatologique; F. DELBARRE, chef de Laboratoire à la Faculté de Médecine de Paris. Paris: Masson. 1953. Pp. 414. Fr. 2800.

So much has been written about cortisone and corticotrophin that their relevance to the everyday needs of medical practice is perceived with increasing difficulty. A comprehensive account of their use in rheumatic disease, where they were first applied, is timely, and Professor Coste and his associates in Paris have produced a useful account of hormone therapy in this field. It is based on the study of 460 patients of their own, of whom a third had rheumatoid arthritis, and a fifth had rheumatic fever. The indications, dosage, and prognosis are carefully assessed, and particular attention is given to the management of relapses. In rheumatoid arthritis, and Still's disease, the use of concomitant gold therapy is described, but the authors are guarded about its value; gold therapy following hormone treatment is not favoured. In rheumatic fever corticotrophin is represented as a great advance in treatment, arresting the progress of cardiac damage to a significant extent. Professor Coste and his colleagues are aware that "quelques-uns, en Angleterre surtout, restent sceptiques," and they make no final judgment, awaiting the results of later follow-up. Indeed, in striving to honour impartiality, they have added considerably to the length of their book. Methods and cases are described very fully, so that comparison may be made with the American and other European authorities quoted, and a bibliography of 28 pages is witness to diligence in this respect. The practical value of the book perhaps suffers through this prolixity, but it is nevertheless a welcome account of this important subject.

Advances in Cancer Research

Vol. 1. Editors: JESSE P. GREENSTEIN, National Cancer Institute, U.S. Public Health Service, Bethesda, Maryland; ALEXANDER HADDOW, M.D., D.SC., Chester Beatty Research Institute, Royal Cancer Hospital, London. New York and London: Academic Books. 1953. Pp. 590. 96*s*.

THE present volume is the first of a series designed to reflect the "steady and inevitable march of the tides of our knowledge and increasing understanding" of cancer. This tidal metaphor is based on the "mysterious and inexplicable ebb and flow of ideas and experimental approaches" to this widely ranging subject. First acquaintance with the series shows that it is not intended for the general reader but rather for almost as many experts as there are individual chapters.

Included are reviews of electronic configuration and carcinogenesis; epidermal carcinogenesis; the milk agent in the origin of mammary tumours in mice; hormonal aspects of experimental tumorigenesis; properties of the agent of the Rous no. 1 sarcoma; applications of radio-isotopes to studies of carcinogenesis and tumour metabolism; the carcinogenic aminoazo dyes; the chemistry of cytotoxic alkylating agents; nutrition in relation to cancer; and plasma-proteins in cancer. All are written by specialists in their own branch, 6 from the U.S.A. and 4 from Britain. Most of the contributions are comprehensive and objective, so much so that Reviews would be a more fitting title than Advances. Subject and author references and indexes are extensive.

The chapter on nutrition in relation to cancer is one that all workers, whatever their specialty, will need to consult. One omission here may be regretted—that is the paper, a model of its kind, by J. C. Drummond in the *Biochemical Journal* (1917).

Those who are new to experimental mammary cancer would be greatly assisted if contributors would make clear whether the work they are referring to was done with or without the milk factor. Frequently this was not yet known at the time, by the experimenters themselves. Usually it is possible in the reviews in this volume to find out; but as the point is an essential one it might often be more clearly made.

The series should be very useful to all who are trying to find their way about the subject.

THE LANCET

LONDON: SATURDAY, JUNE 27, 1953

Cardiac Catheterisation

SOME twelve years have passed since COURNAND and RANGES [1] began to describe results of right atrial catheterisation; and it is nearly a decade since MCMICHAEL and SHARPEY-SCHAFER [2] began to report on the application of the procedure in this country. Regarded at first with some suspicion and reserve, cardiac catheterisation quickly found a very important place in the selection of cases of cyanotic congenital heart-disease for operation. Every cardiac centre where surgery is undertaken now has a laboratory for catheterisation and allied procedures, such as angiocardiography,[3] and for related studies of pulmonary function. The old cardiologist with his quiet and mild stethoscopic and electrocardiographic studies has been replaced by a highly organised team surrounded by complex and expensive laboratory equipment. The cardiac laboratory is a hive of industry; here clinical investigation and research go hand in hand, and every obscure cardiac problem is illuminated—or sometimes made more difficult—by a mass of hæmodynamic data. Technical advances have been applied with alacrity. Instantaneous optical and other similar pressure-recording devices are now in routine use; and in cases of congenital heart-disease angiocardiography with special radiographic equipment is undertaken at the same time as catheterisation. Recently oximeters have been developed which, by transillumination of the ear on to a sensitive photocell, provide immediate information about the oxygen content of the blood, or even a continuous record of its changes. Moreover, the oximeter can be readily used to study the passage through the circulation of innocuous blue dyes after their rapid injection either into a peripheral vein or through a catheter into the heart itself. By this means intracardiac shunts may be recognised; and, where the heart is of normal configuration, the time of passage of the dye permits the estimation of intrathoracic blood-volume (mainly in the lungs).[4]

The place of cardiac catheterisation in congenital heart-disease and in other diagnostic cardiac problems is well reviewed in a Mayo Clinic symposium.[5] By intensive investigation of various types of pressure-recording systems a strain-gauge system has been found to give the most accurate reading of pressures and greatest freedom from artefacts. The report emphasises the value of catheterisation studies combined with intracardiac injection of dye. In the presence of a right-to-left intracardiac shunt, dye appears in the systemic vessels much more rapidly than dye passing through the lungs. Study of the curves of dye concentration may thus be of great value in locating the site of a shunt. Necropsy studies of hearts previously catheterised showed, however, that data from catheterisation could be confusing or even misleading. For example, slight patency of a foramen ovale may sometimes be important, and yet difficult or impossible to recognise by catheterisation.

Cardiac catheterisation has won an unassailable place in relation to these special problems of cardiac surgery, but knowledge of its risks has also increased. In the earlier years most investigators were satisfied with pressure measurements and blood samples from the right atrium, and little harm seems to have resulted.[6] Gentle passage of the catheter along ever-widening veins into the middle of a roomy right atrium need cause no trauma. But when the operator decides to probe beyond this, round the bend of the right ventricle and pulmonary artery and into as many accessible chambers as possible, in deformed and diseased hearts, it is not surprising that trouble may arise. The Mayo Clinic pathologists saw sub-endocardial hæmorrhage in 2 of 28 catheterised hearts in cases where the patient had died from other causes. Limited local thromboses in the arm veins and transient arrhythmias during catheterisation are common. The Mayo Clinic workers report 2 deaths and 4 cases of more persistent arrhythmia in 474 catheterisations. On the other hand, 3 patients died while awaiting the investigation, and other recorded deaths have usually been in seriously ill patients. MCMICHAEL and MOUNSEY [7] have recorded precordial pain and collapse, probably resulting from passage of the catheter into the coronary sinus. HEBERT et al.[8] report a hæmatoma at the mouth of the coronary sinus in one case and hæmopericardium in another. Pyrogenic reactions are difficult to avoid completely, and in seriously ill patients these can be lethal; while occasionally thrombotic complications may lead to serious embolism. LENÉGRE puts the mortality from catheterisation at 0·7% (7 in 973), but resulting morbidity may be higher. The American Heart Association has appointed a committee to report on catheterisation and make recommendations, and its report will be awaited with interest. Meanwhile, all concerned with this type of investigation will no doubt apply it with full knowledge of both its advantages and its potentially harmful consequences. Technique must be rigorous, with careful precautions against the known complications; and correct indications should be accepted Discrimination is needed, because only a small proportion of cardiac patients require study by catheterisation. The reasons should be precise, agreed by responsible senior staff in consultation, and explained to the patient, who should give consent; and the cardiologist in charge of the patient should himself be responsible for the conduct of the catheter study. Where cardiac-output studies alone will suffice, catheterisation should not go beyond the right atrium, for the minor inaccuracies of mixed venous-blood samples from this

1. Cournand, A., Ranges, H. A. *Proc. Soc. exp. Biol., N.Y.* 1941, **46**, 462.
2. McMichael, J., Sharpey-Schafer, E. P. *Quart. J. Med.* 1944, **13**, 123.
3. See *Lancet*, May 30, 1953, p. 1082.
4. Kepelman, H., Lee, G. de J. *Clin. Sci.* 1951, **10**, 383.
5. *Proc. Mayo Clin.* 1953, **28**, 49, 89.
6. Zimdahl, W. T. *Amer. Heart J.* 1951, **41**, 204.
7. McMichael, J., Mounsey, J. P. D. *Brit. Heart J.* 1951, **13**, 397.
8. Hebert, J., Scébat, L., Lenègre, J. *Arch. Mal. Cœur*, 1953, **46**, 325.

situation are more than counterbalanced by considerations of the patient's safety and well-being. Where other methods of circulatory study, such as the dye techniques, will give sufficient information they should be used in preference to cardiac catheterisation. The presence of expensive equipment occupying valuable space should not determine the type of study pursued. Otherwise, man becomes the slave of his machines.

Nursing Problems in the Provinces

IN our time the training of nurses, though still largely practical, has had a growing academic content; and many have suggested that this trend is becoming too pronounced. Hospitals which find it difficult to get enough recruits of a suitable type are especially apt to complain that the syllabus is too exacting; and indeed, from the administrator's point of view, the obstacles it can present are often serious. The hospital management committee of the Luton and Hitchin group no. 2 have lately approved a report [1] from Mr. R. E. LINGARD, their secretary, which speaks strongly on the subject.

Recruitment to nursing has improved very much in recent years. In 1947 there were 46,655 nurses in training; in 1951 there were 58,270. Since then the figures have levelled off, and it is probable that recruitment has reached its peak. Nevertheless, in Mr. LINGARD's opinion, expansion would still have been possible in "progressive schools and hospitals" but for three changes—one already in action and two still in prospect—in the regulations of the General Nursing Council. On Aug. 1 last year, the G.N.C. fixed the age of entry to nursing training at 18—a rule which we have long advocated and fully support, though there is no doubt that it has placed many hospitals in temporary staffing difficulties. The council have also drawn up a new syllabus, to come into force in January of next year, which increases the time spent by the student nurse in the classroom; and have announced their intention, at a date not yet specified, of raising the educational standard required of entrants. Mr. LINGARD believes that a year ago, before the new age of entry was enforced, the only reason why hospitals in his group could not enlarge their nursing staffs was lack of residential accommodation. For the past eight months, however, recruitment in this group has not kept pace with losses. This he attributes largely to the raising of the age of entry from $17\frac{1}{2}$ to 18. He argues that if girls of $17\frac{1}{2}$ formed 20% of the hospitals' intake in the past, this change of policy means a permanent reduction of 3000–4000 in the number of students working in hospitals. But a girl who is not accepted for training at $17\frac{1}{2}$ does not dissolve into air: she is usually still there six months later, and her wish to nurse may well have survived the interval, particularly if she is able to take a pre-nursing course and to complete part I of her preliminary examination before she enters hospital. It was inevitable that recruitment to hospitals formerly taking girls at $17\frac{1}{2}$ should drop seriously during the first six months after enforcement of the new rule; but we must wait for the figures for the second six months before we can say whether recruitment has been permanently injured.

1. Some Current Problems of Nurse Training. Luton and Hitchin Group No. 2 Hospital Management Committee Report M.C.7/53.

Like the rest of us, Mr. LINGARD has been much impressed by the finding of the Nuffield Job-Analysis Team [2] that three-quarters of the time spent on nursing duties in the wards is contributed by student nurses. So long as this is the case, he argues, and so long as the greater part of the student nurse's time is spent in giving service to the hospital, as distinct from receiving tuition, her real status is something between that of an apprentice and one serving articles, and not that of a student. He therefore regards with misgiving any measures which lead "to an undue increase in the time spent in classrooms, with a consequential loss in the time spent in wards." It is easy to understand his anxiety—the anxiety of the administrator who has to see that beds are staffed and patients nursed. But it would be unfortunate if, at a time when all other countries are steadily advancing the standard of training and status of their nurses, we—the pioneers—reduced ours to the level of so many pairs of hands. A nurse fit to take responsibility in modern wards cannot be bred by the *practice* of ward work alone: she must have a theoretical training, and the time at present allowed to her for this purpose is small.

It is true, of course, that a nurse engaged in the routine tasks required to keep her patients comfortable does not necessarily need a high standard of academic ability or training. But that is why the grade of State-enrolled assistant nurses (S.E.A.N.) was set up—to keep within the nursing team the girl who has no academic gifts but has a natural bent for nursing. The nursing orderly, too, can be used in the team to supplement the nursing staff. Thus hospitals with recruitment difficulties are now in a position to consider a new staffing structure. If they cannot attract enough entrants of adequate educational standard they can either supplement their students with orderlies, or turn over to the training of S.E.A.N.s instead of S.R.N.s. Unfortunately, such a change in the type of training offered is felt to entail a loss of face. It also means, for the matron, a financial loss, for matrons of S.E.A.N. training-schools receive a slightly lower rate of pay than matrons of schools training S.R.N.s. This pointless distinction should surely be obliterated; and it is to be hoped that the nursing profession will themselves get that done. If the G.N.C. do raise the educational standard required of entrants it is probable that many hospitals will find it convenient to make this change. The proposed standard is still under consideration; it will probably be that reached by the ordinary girl leaving a secondary (grammar or modern) school at the age of 15.

We are looking towards a new structure in nursing, built on the notion of the nursing team. There will be room in it for women of high academic, technical, and administrative ability; for responsible women who combine gifts for ward management, clinical nursing, and the teaching of juniors; for comfortable competent bedside nurses with no academic pretensions; for intelligent orderlies attracted by an interesting job; and for students in training for either the register or the roll. It has always been a profession offering scope for many talents, but now the opportunities are expanding horizontally as well as vertically.

2. The Work of Nurses in Hospital Wards. London: The Nuffield Provincial Hospitals Trust, 1953. See *Lancet*, Feb. 21, 1953, p. 379.

Treatment of Renal Tuberculosis

THE treatment of renal tuberculosis has been modified but not revolutionised by antibiotics. These new weapons, which are still being developed, are likely to play an increasingly effective part in the war against tuberculosis; but they have certainly not rendered obsolete the older weapons—constitutional treatment and surgery. They have indeed had the opposite effect by showing up the continuing need for constitutional treatment and the advantages of surgery. As COSBIE ROSS and his colleagues [1] remark, these three weapons are complementary, and surgery is only an incident in the course of treatment. The crude doctrine of Alberran, epitomised in the equation *tuberculose rénale=néphrectomie immédiate*, is based on a false conception of the disease by which the tuberculous process was regarded as starting as a solitary focus in one kidney and spreading from there to the rest of the renal tract, including the opposite kidney. It is far more probable that the disease starts in scattered hæmatogenous foci in both kidneys and that the macroscopic "solitary" focus is merely one of these lesions which has developed, the others having healed or become quiescent. In these circumstances nephrectomy for tuberculosis cannot be viewed as a radical operation, and the concept of *néphrectomie immédiate* gives place to that of *néphrectomie opportune*, in which the operation is delayed until constitutional measures and antibiotics have brought the infection as far as possible under control.

There is evidence that streptomycin can heal the small closed parenchymatous focus, but not the established caseocavernous lesion.[2] Fibrosis is a feature of the untreated tuberculous lesion, making an avascular wall around the lesion which hinders the access of blood-borne therapeutic agents. Streptomycin, by increasing this fibrosis, impedes its own action. In urinary tuberculosis the contraction of such fibrous tissue has other untoward effects, such as ureteric obstruction and vesical contracture. Altogether this action of streptomycin must be reckoned a serious defect, and it is encouraging to see the results of histological studies of the effects of isoniazid on tuberculous renal lesions, lately described in these columns by Dr. DICK.[3] One of the most striking findings was the absence of fibrosis in the more recent lesions in cases treated with isoniazid only. Even the old fibrotic lesions showed revascularisation, in striking contrast to cases treated with streptomycin and to untreated cases. Moreover isoniazid seemed to arrest caseation and even to promote absorption of caseated material. Thus isoniazid put the tuberculous process, so to speak, into reverse; but unfortunately this improvement was not maintained after three months' treatment in cavities and in open lesions of the calyces and pelvis; here there were signs of reactivation. These histological findings correspond with the clinical impression that the improvement brought about in the first three to six weeks of isoniazid treatment is not maintained. According to in-vitro bacteriological evidence tubercle bacilli resistant to isoniazid quickly appear; but this complication can be retarded by combining isoniazid with streptomycin. Moreover DICK found evidence that isoniazid reversed some of the fibrotic changes even in chronic lesions previously treated with streptomycin. Thus it seems that these two drugs are to some extent complementary.

Nephrectomy is still the standard surgical treatment of renal tuberculosis when the other kidney is free from infection or only slightly infected. This measure is based on the sound principle that a resistant tuberculous focus is best removed when this is anatomically and physiologically feasible. At a conservative estimate nephrectomy more than doubles the chance of cure; and the antibiotics have not much altered this, for although they have improved the results of non-surgical treatment they have also greatly improved the results of nephrectomy, particularly by promoting smooth healing after operation. Nevertheless the limitations and disadvantages of nephrectomy are obvious. The operation is at the same time too radical and not radical enough: it is too radical if the kidney contains healthy tissue, as is very commonly the case; and it is not radical enough because it leaves untouched the original extra-urinary focus, and possibly also small foci of disease in the other kidney. On these grounds there is a clear prima-facie case for partial nephrectomy; and SEMB,[4] in an account of 87 cases treated by this method, shows that this is both feasible and successful. SEMB compares renal with pulmonary tuberculosis in regard to pathological anatomy and surgical treatment. In both conditions small parenchymatous foci may heal, especially with the help of antibiotics; but cavities (the ulcerocavernous or caseocavernous lesions of renal disease) are much less likely to heal, especially in the kidney. Twenty years ago the surgical treatment of a solitary cavity in the lung which resisted lesser measures might have been total thoracoplasty; nowadays it would probably be segmental resection. A solitary caseocavernous lesion of a kidney is still usually treated by total nephrectomy; and SEMB considers this unjustifiable. The results of partial nephrectomy in his hands are, from the point of view of cure, at least as good as those of total nephrectomy. There is one reservation: none of his cases has yet been followed for more than five years, but even so the results are excellent. There have been no deaths, and the general condition of all the patients is satisfactory; in nearly 90% the urine remains free from evidence of tuberculous infection. In only 2 cases did the function of the partially resected kidney fail; and the series includes 13 cases in which part of the only remaining kidney was removed. These results at least justify a thorough trial of this method.

Partial nephrectomy is not a new operation. It was first performed as long ago as 1887 by CZERNY (for tumour), but until recently it was only rarely done. In 1937 GOLDSTEIN and ABESHOUSE [5] collected a series of 290 reported cases and described 6 of their own. Only 41 of these operations were for tuberculosis, and the results were poor; of the 41 patients, 5 died, 5 developed a urinary fistula, and 6 required a secondary nephrectomy. The operation was much more often and more successfully done for stone; and hitherto it has been practised mainly for this disorder. Of 155

1. Ross, J. C., Gow, J. G., St. Hill, C. A. *Brit. med. J.* April 25, 1953, p. 901.
2. Jacobs, A., Borthwick, W. M. *Proc. R. Soc. Med.* 1950, **43**, 453.
3. Dick, J. C. *Lancet*, April 25, 1953, p. 808.
4. Semb, C. *J. Oslo City Hosp.* 1953, **3**, 45.
5. Goldstein, A. E., Abeshouse, B. S. *J. Urol.* 1937, **38**, 1.

partial nephrectomies reviewed by HANLEY [6] in 1950, 125 were for stone and only 8 for tuberculosis. Many patients in this series were operated on before the advent of streptomycin; this antibiotic has widely extended the field of partial nephrectomy, especially for tuberculosis because of its effectiveness against tuberculous infection of the wound. In total nephrectomy for tuberculosis the minimal requirements are that one kidney is tuberculous and that the other is free from infection and functioning adequately. For partial nephrectomy, more precise information is essential. The details of renal anatomy are of prime importance—particularly the arrangement of the calyces, with its variations, and the blood-supply. SEMB adopts FÖLGREN's scheme, according to which the kidney has seven pairs of pyramids, dorsal and ventral. These pairs are grouped into three divisions; the uppermost three pairs constitute the upper division, and the remaining four pairs are divided equally between the intermediate and lower divisions. In addition to this, there are six different ways in which the pelvis may branch to make the calyces of the middle division. The ramification of the renal artery and vein varies considerably, especially outside the kidney. SEMB's scheme of pathological anatomy divides tuberculous renal disease into three groups.

In the *first group* there are small tubercles or tuberculous infiltrations which may lead to the excretion of tubercle bacilli in the urine, but in which there is no macroscopic destruction and especially no open communication with pelvis or calyx. This he calls the "parenchymatous" group, and it is not a surgical problem. For one thing this type of lesion may now often be cured by medical treatment; and for another it does not lend itself to pyelographic study, so that a detailed anatomical diagnosis cannot be made.

The *third group* he terms the "total destructive," in that all three divisions of the kidney are macroscopically affected and often the ureter is also involved. Obviously partial nephrectomy has no place here.

The *second group*, termed "local-destructive," is the group for partial nephrectomy. Here the macroscopic destruction may involve as little as one part of one pyramid or as much as two complete divisions of the kidney.

This second group constitutes no less than 56% of all cases of renal tuberculosis in SEMB's series—which shows how important a part may be played by partial nephrectomy.

By SEMB's scheme, which he describes as selective medical-surgical treatment, the patient always undergoes preliminary sanatorium treatment, which may last as long as six months if there are other active foci or the general condition is poor. Antibiotics are used sparingly in this phase, streptomycin being restricted to a total amount of 15 g. In the post-operative phase a rather larger amount is allowed—up to 40 g. in uncomplicated cases. If operation on extra-urinary lesions is necessary, this is done before the operation on the kidney. The renal lesions are accurately charted by means of excretion and instrumental pyelography. Aortography is also much used; WEYDE,[7] the radiologist associated with SEMB, has described the technique and results. He emphasises the importance of the "nephrographic" effect, which maps out the areas of non-functioning parenchyma, in addition to the more obvious effect which delineates the individual vessels.

Ample exposure is necessary for partial nephrectomy, and SEMB favours access through the bed of the eleventh or twelfth rib.

A bloodless field may be obtained either by clamping the pedicle or by compressing the renal substance; but SEMB found when operating on cases with a sole remaining kidney that the renal function took a harder knock when the pedicle itself was clamped. In his series the extent of the resection varied greatly from case to case, and in 95% of cases the lesion or lesions were removed in one block of tissue; the upper division was involved more than twice as often as the lower. The pelvis or neck of the calyx is sutured (in contrast to STEWART's [8] advice when operating for stone); and the vessels are dealt with mainly by ligature in the cut surface of the kidney, and more rarely by securing individual vessels in the hilum. The cut surfaces are sutured with a double row of catgut, the outer row getting a hold on the capsule; no fat or muscle appears to be used as a further safeguard against hæmorrhage.

Postoperative complications have been remarkably few, consisting in wound infection (3 cases) and failure of function of the remaining tissue (2 cases); there has been no urinary fistula and no postoperative hæmorrhage.

These good results show that in the immediate postoperative phase partial nephrectomy can be no less safe and satisfactory than total nephrectomy. It is reasonable to expect that the late results will also be good, in view of the excellent showing at five years; for we know that after total nephrectomy 75% of the deaths occur within five years. The least that can be said is that here is a method of surgical treatment which is based on sound principles, conserves functioning tissue, and gives promise of improved results.

6. Hanley, H. G. *Proc. R. Soc. Med.* 1950, **43**, 1027.
7. Weyde, R. *J. Oslo City Hosp.* 1951, **1**, 269.
8. Stewart, H. H. *Ann. R. Coll. Surg. Engl.* 1952, **11**, 32.

Annotations

COMFORTABLE CHILDBIRTH

THE Government's campaign to ensure that every midwife shall know how to give gas-and-air analgesia for the relief of pain in childbirth has eventually been very successful. By the end of 1951, 94% of all midwives in England and Wales had been trained in the use of the method; and the National Birthday Trust Fund, as Mr. William Penman, the acting chairman, points out,[9] have done much to ensure that enough machines be available. He has analysed the official figures of domiciliary confinements attended by midwives in 1951, to show how many of the mothers received gas-and-air analgesia. The results show a wide variety of practice throughout the country.

There were 253,069 domiciliary confinements attended by midwives during the year; in 192,529 of them the midwife acted as midwife, and in 60,540 as maternity nurse. Analgesia was given in 60% of the first of these two groups and 51% of the second. Of the 146 administrative units in the country, 1 reported that confinements in which analgesia was given amounted to only 8% of the total, and in another 2 the figure was only 16%. At the other end of the scale, 15 units reported figures of 80–90%, and 5 others over 90%. The mean for the country as a whole was 58%.

Clearly it is one thing to train a midwife in the use of this method, and another to get her to use it. From the wide variation in the figures up and down the country it seems that she may be influenced by something more than the views of the mother—perhaps by the views of the medical officer of health. It would be convenient to know just how often relief in childbirth is really needed: medicine sorely lacks a handy little machine

9. *Publ. Hlth*, 1953, **66**, 79.

to measure and compare the interpretation of pain by different subjects. Childbirth presents peculiar difficulties. As Mr. Penman himself points out, we know that in a proportion of cases women either do not need, may not have, or refuse to accept analgesia; but he thinks this proportion is a small one. The average of 58% of administrations of analgesia is, he thinks, "much too low"; and it is very hard indeed to know whether he is right. Those experienced in training mothers to relax, in preparation for confinement, say that it is often possible to ensure a painless labour without analgesia. Many hospitals and antenatal clinics nowadays arrange classes in which mothers learn to exercise the voluntary muscles concerned in labour, as well as how to relax; and are also taught a little about their own physiology. We have lately mentioned the scheme of this kind run by Prof. W. C. W. Nixon's team at University College Hospital.[10] The Maternity Centre Association of New York holds an elaborate course, which includes not only exercises but also lectures, attended by both mothers and fathers, on the anatomy and physiology of reproduction. They have published a set of clear illustrations of the exercises, which are based on those of the late Helen Heardman.[11] The lecture course ends with a "labour rehearsal," in which the whole birth process is reviewed, and the parents are given the chance to ask plenty of questions. Thus prepared for the birth, mothers feel little fear, and avoid much of the pain associated with anxiety and tension.

It would be unfortunate if our concern over the pangs of labour diverted our attention from the mother as a whole. The Family Planning Association, in a sensible pamphlet,[12] put the picture in proportion. Anæsthesia or analgesia, they say, can render even the most difficult labour nearly painless, and the mother will wake to find her baby comfortably born. But, they add, it must not be forgotten that many women find childbirth an exhilarating experience, which, though hard work, is not attended by pain; and the question arises whether "this taking of the birth-process out of the mother's control produces in her the same feeling of accomplishment as when she has consciously coöperated in the birth of her child." The Birthday Trust Fund wish to see enough gas-and-air analgesia machines available, and enough midwives trained in their use, for every mother who asks for it to have relief in childbirth. It is not possible, without further research, to say what proportion do ask for it at present, still less how many need it, or whether fewer would need it if more were prepared for childbirth on the lines followed at University College Hospital. A rate of 8% of administrations is almost certainly unkindly low; but a rate of over 90% may be equally unkindly high. Training in relaxation takes time and trouble; analgesia is in some sense a short cut. If our aim is to do the best we can for the mother we must take all her needs into account, neither exposing her to wasteful needless pain, nor deposing her too officiously from control of her great occasion.

VEGETABLE JUICES

JUICES obtained by pressing vegetables in special apparatus have attracted little interest in Britain. They have been popular, however, in America as beverages or cocktails, and in German-speaking Continental countries as therapeutic agents. Dr. H. E. Magee,[13] of the Ministry of Health, has studied the evidence favouring the use of juices for either of these purposes. With the coöperation of Mr. Russell Allen, PH.D., he has also collected further information on the chemical composition and nutritional value of juices pressed from many common vegetables, including broccoli leaves, cabbage, carrots, celery, kale, melon, parsley, spinach, tomato, and watercress.

All the juices examined contained sugars, but in widely divergent amounts. Thus carrot juice contained 7·11%, estimated as glucose, in contrast to only 0·2% in the juice of watercress. Equally large variations were found for minerals. Thus iron averaged 2·12 mg. per 100 ml. in watercress and 0·08 mg. in tomato; calcium averaged 18·7 mg. in broccoli leaves and only 0·75 mg. in spinach. Vitamin B_1 was richest in cabbage juice, but this vitamin was completely absent from spinach juice. These divergencies may be traced partly to corresponding variations in the unpressed vegetables, for which Magee quotes official data, and partly to variations in the efficiency with which the nutrients are passed into the juice. Probably the low calcium contents of spinach juice may be related to the high concentration of oxalic acid in this vegetable, which may immobilise calcium in the form of its insoluble oxalate. On this idea it is difficult to explain, however, either why iron should be included fairly freely in the juice or why vitamin B_1 should be excluded. Too much faith, of course, cannot be placed in comparisons on sets of data which were obtained on the juice and unpressed vegetables on different occasions. Thus in order to reconcile the value of 3% found for sugar in broccoli juice with the value of 0·4% quoted for the unpressed vegetable we must suppose an efficiency of extraction which appears almost impossible. From 100 g. of leaves not more than 13 ml. of juice would have to be pressed, and this small volume of fluid would have to carry the entire sugar contents of the original material.

The antiscorbutic power of fresh vegetables is one of their most important nutritional virtues, and vitamin C might be expected to appear in the juice in company with other water-soluble substances. It is well known, however, that when plant cells are damaged they liberate enzymes which destroy the vitamin. High pressure would obviously rupture the cells and the juices would be expected to have antiscorbutic activity only if consumed very promptly, or if effective steps were taken to stabilise the vitamin. Since many of Allen's analyses for ascorbic acid were made several days after the expression of the juice it is not surprising that most specimens were quite inactive. A striking observation, however, was made on kale juice, which had retained no less than 46 mg. of ascorbic acid per 100 ml. By contrast, a specimen of cabbage juice, freshly prepared by Mr. V. L. S. Charley, contained only 8·5 mg. per 100 ml. Magee suggests that either kale does not contain ascorbic acid oxidase, or an anti-enzyme is present. Further attention to this interesting point seems highly desirable. Substantial amounts of carotene were found only in juices from carrots and watercress.

Reports that vegetable juices are effective in the treatment of obesity and allied conditions, such as hypertension, disease of the gall-bladder, and cardio-vascular disturbances are explained by Magee on the assumption that dosing with juice is usually accompanied by a strict curtailment of the food intake. He attributes the benefits ascribed to vegetable-juice therapy in rheumatic conditions to their general nutritive value, although it is difficult to see what advantages they would have over the unpressed vegetables. He seems prepared to accept the strong claims of Cheyney[14] and others that large doses of juice, particularly from the cabbage, are effective in the treatment of gastro-intestinal disorders. Presumably the pectin present in raw juices absorbs toxic substances and bacteria from the bowel.

10. *Lancet*, April 25, 1953, p. 833.
11. Reminder Sheets for Exercises in Preparation for Childbearing. Maternity Centre Association, 654, Madison Avenue, New York 21, N.Y., U.S.A. Pp. 32. $2·50.
12. Pain Relief in Childbirth. Family Planning Association, 61, Sloane Street, London, S.W.1. Pp. 12. 6*d.*; 8½*d.*, postage paid.
13. Magee, H. E. *Mon. Bull. Minist. Hlth Lab. Serv.* 1953, **12**, 78.
14. Cheyney, G. J. *California Med.* 1949, **70**, 10; *J. Amer. diet. Ass.* 1950, **26**, 668.

In his own experiments he has proved the high buffering power of vegetable juices against acids. Spinach extracts are superior to milk in their buffering power, and would therefore be expected, for theoretical no less than for practical reasons, to be valuable in the treatment of gastric hyperacidity.

Despite these virtues Magee sees little future for the consumption of vegetable juices by healthy persons. Even the best pressed juices, unlike purées, contain only small fractions of the nutrients present in the original vegetable. The residue after pressing, moreover, contains not only assimilable nutrients but roughage which assists peristalsis. There seems to be no scope in this country for the more extensive use of vegetable juices, except as components of invalid diets and as occasional cocktails.

CHEMOTHERAPY OF ACTINOMYCOSIS

BEFORE the introduction of sulphonamide therapy actinomycosis caused by the anaerobic *Actinomyces israeli* was treated principally with potassium iodide; and even now, probably because of its effect on the granulomatous infiltration, this is sometimes a useful adjunct to the antibiotics.

Early results with the sulphonamides in the treatment of actinomycosis seemed very successful; but apparent cure was sometimes followed by relapse, and even long courses of carefully controlled treatment were often unsuccessful. The application of antibiotic therapy was attended by many dramatic cures, even in very severe cases; and soon penicillin eclipsed the sulphonamides. Continued use of penicillin, however, brought a crop of failures. Many of these were due to inadequate initial dosage with which the infecting micro-organism became resistant. This danger was largely averted by giving massive doses in the initial stages. Garrod [1] showed by in-vitro tests that each of the five antibiotics in common use—penicillin, streptomycin, aureomycin, chloramphenicol, and oxytetracycline (terramycin)—are bacteriostatic to strains of *A. israeli*. Streptomycin, aureomycin, and chloramphenicol have been administered chiefly in cases where penicillin had already failed; and often one of these three has effected a remarkable cure. This does not imply, however, that any of the three is always superior to penicillin: the antibiotic that is the most effective in one case may be the least effective in another. Kelly [2] described a case of abdominal actinomycosis in which, after unsuccessful treatment with penicillin in large doses, sulphadiazine, and streptomycin, clinical improvement was obtained with chloramphenicol; but relapse ensued, and eventually cure was rapidly effected by administration of aureomycin. In another case, reported by Torrens and Wood,[3] streptomycin arrested the disease after penicillin, the sulphonamides, iodides, and surgical measures had failed.

It seems possible that the infecting strains of *A. israeli* may differ in their sensitivity to particular antibiotics; but a preliminary sensitivity test of the culture against the individual antibiotics should enable the most suitable to be chosen. So far the newer antibiotics have had only a very limited trial in the initial treatment of actinomycosis; so a fair comparison with penicillin is not feasible. The first important therapeutic trial of oxytetracycline in actinomycosis is reported by Lane et al.[4] who successfully treated with it 7 cases of the oro-cervico-facial type of the disease. The disease, which was of dental origin and in some cases followed extraction of teeth, was in the lower jaw and was related to the molars and bicuspids; it was localised and acute; its average duration before the start of treatment with oxytetracycline was only five and a half weeks. Suppuration occurred in all cases, and *A. israeli* was isolated in culture from the pus. In 6 of the patients the disease was rapidly cured by oxytetracycline in doses of 500 mg. by mouth every six hours for adults, with proportionately smaller doses for children; treatment was continued for from two to six weeks. Of these 6 cases, 3 had previously been treated unsuccessfully with penicillin, and 1 had become penicillin-resistant. The 7th case was treated at first with penicillin and chloramphenicol and responded well to the latter; but an urticarial rash appeared and the treatment was stopped. Six weeks later, oxytetracycline was given in doses of 250 mg. every six hours for eight days, and this short course of treatment brought about apparent clinical cure. The disease recurred eight weeks later, but it responded well to a further course of oxytetracycline in doses of 500 mg. every six hours, supplemented by small doses of potassium iodide.

Another group of drugs has proved useful in treating actinomycosis. Schoenbach et al.[5] reported encouraging results from the treatment of 3 cases of blastomycosis (*Blastomyces dermatitidis*) with stilbamidine intravenously and propamidine applied locally to the lesions. A diet low in protein and purin is advisable during this treatment. Miller et al.[6] treated a case of actinomycosis of the jaw with stilbamidine injected intravenously at rather longer than daily intervals, starting with 0·05 g., which was increased rapidly to 0·15 g., in 200 ml. of 5% glucose solution. The first course lasted three weeks; and, after an interval of sixteen days, a second course was given over a period of two weeks, which resulted in apparently complete clinical recovery. This patient had previously been treated unsuccessfully with procaine penicillin and sulphonamides. Another agent, pregnenolone acetate, was used with success by Lamb et al.[7] in treating a local infection by an acid-fast actinomycete (*Nocardia* sp.) in a girl aged 6. No indication of toxicity or metabolic disturbance was found after a total dosage of 60 g. given over a period of eight months.

COLONIAL HEALTH SERVICES

IN the Colonial territories increasing population, urban concentration, improved transport, and ever more lively awareness of the benefits of Western medicine are straining the medical services, especially in the main centres. Thus in Singapore the annual hospital out-patient attendance, which averaged 90,000 immediately before the late war, is now approaching 600,000; and in some maternity wards deliveries number about 90 per bed per annum. As regards medical staff, a high rate of recruitment from the United Kingdom and other Commonwealth countries was achieved in 1951; and the latest Colonial Office report [8] records that this rate was maintained in 1952, when 147 doctors were appointed (18 for West Africa, 42 for East and Central Africa, 47 for South-east Asia, 24 for the West Indies, 9 for the Pacific area, and 7 for other territories). In addition medical officers of local origin are steadily increasing, particularly in the Far East, West Africa, the West Indies, Cyprus, and Mauritius; and at the end of January this year 638 Colonial students were studying medicine in the United Kingdom or Eire. The number of specialist posts has been increased; it has proved impossible to fill all such posts from within the service, and, notably in the fields of radiology, anæsthetics,

1. Garrod, L. P. *Brit. med. J.* 1952, i, 1263.
2. Kelly, H. H. D. *Ibid*, 1951, ii, 779.
3. Torrens, J. A., Wood, M. W. W. *Lancet*, 1949, i, 1091.
4. Lane, S. L., Kutscher, A. H., Chaves, R. *J. Amer. med. Ass.* 1953, **151**, 986.
5. Schoenbach, E. B., Miller, J. M., Long, P. H. *Ann. intern. Med.* 1952, **42**, 31.
6. Miller, J. M., Long, P. H., Schoenbach, E. B. *J. Amer. med. Ass.* 1952, **150**, 35.
7. Lamb, J. H., Kelly, F. C., Shackleford, P. O., Rebell, G., Koons, R. C. *Arch. Derm. Syph., N.Y.* 1953, **67**, 141.
8. Colonial Office: The Colonial Territories, 1952–53. Cmd. 8856. H.M. Stationery Office. Pp. 157. 5*s*.

pathology, and psychiatry, it has even been difficult to recruit from the United Kingdom.

In most territories the full approved establishment has been reached or nearly reached; but this does not mean that needs are being fully met. As the report remarks, industrialisation, with its corollaries of migration of labour and the creation of new urban centres, has especially serious health implications in countries where tropical diseases are endemic and where local customs have not yet been fully adapted to the change from a predominantly rural economy. While the peoples of the various territories are turning with growing eagerness to the curative services, the trained personnel are growingly aware that in the long run their time might be more fruitfully spent on preventive action—and the report describes some striking instances of such action. A somewhat similar situation prevails in every country; but it is especially clear in the Colonies, where doctors are too few and there is great scope for prevention of endemic disorders. These two conflicting calls cannot be satisfactorily met without further expansion of the medical and allied services; and such expansion will depend chiefly on the recruitment and training of personnel from the territories concerned.

THE LISTER INSTITUTE

GOOD wine, it is said, needs no bush; and the governors of the Lister Institute do nothing to vaunt the distinguished work that proceeds under their ægis. Their latest report,[1] no less sober than its forerunners, records that during the past year Dr. A. A. Miles has taken up the directorship of the institute, and that Prof. W. T. J. Morgan, F.R.S., who heads the biochemistry department, has taken over the duties of deputy director.

Professor Morgan and Miss W. M. Watkins, PH.D., have been examining the reactivity of saline extract of certain plant seeds against human red cells of known phenotype, and have studied the inhibition of these reactions by preparation of the human blood-group substances and simple sugars of known constitution. It appears that L-fucose is of greater importance for H specificity than for A and B specificity, and that the N-acetylchondrosamine configuration may play an important part in A specificity. In another department Miss J. M. Horton, PH.D., has continued her work on the chemical fractionation of *Hæmophilus pertussis*, to extract the protective immunising antigen.

Polysaccharides extracted for formamide, alone or in conjunction with globulin, proved to be inactive although preliminary experiments had indicated some activity. The protective antigen, previously shown by F. L. G. Masry to be distinct from the hæmagglutinin and the toxin of *H. pertussis*, now appears to be distinct from the agglutinogen also. The protective action of rabbit antisera to the whole bacillus is unaffected by absorption with purified agglutinogen; and purified agglutinogen will not immunise mice actively. Alkaline extracts of *H. pertussis* yield a polypeptide antigen that appears to be antigenically pure agglutinogen. Variation in the potency of protective antisera with the route of administration of antiserum and infecting dose indicate that more than one type of antibody is concerned.

Dr. L. H. Collier, continuing his investigation of methods of preserving vaccinia virus, has found that purified virus freeze-dried in 5% peptone yields 100% successful primary vaccinations after storage for four months at 37°C. Such a vaccine can be manufactured economically, and is shortly to be tested on a large scale. Should the trial prove successful, it is hoped to issue to tropical countries dried vaccine instead of the lanolinated lymph used at present. The dried vaccine would also be useful for epidemic reserves.

These and many other investigations are mentioned in a report that sets a standard in meiosis.

1. The Lister Institute of Preventive Medicine: Report of the Governing Body, 1953. Issued by the institute, Chelsea Bridge Road, London, S.W.1.

MÉNIÈRE'S DISEASE

IN 1861 Prosper Ménière,[1] a French physician, reported the case of "a girl who, journeying on the box seat of a stage-coach, became as a result of the cold suddenly and completely deaf." Her main symptom was vertigo, and she died on the fifth day. Necropsy showed a "red, plastic matter, a sort of bloody exudate" in the inner ear. Many years later Hallpike and Cairns[2] found in 2 cases of Ménière's disease dilatation of the whole of the membranous portion of the inner ear—so-called hydrops of the labyrinth. This change has since been repeatedly confirmed; but its cause is still undecided. The suggested causes include disturbances of water and salt metabolism, vitamin deficiencies, allergy, and toxic labyrinthitis from a septic focus. According to the belief, the patient is deprived largely of fluid and wholly of salt, fed on vitamins or filled with anti-histamine drugs, or asked to submit to operation for the drainage of infected sinuses or the removal of teeth or tonsils. With these various régimes relief is common, but cure rare; and simple sedation is the chief medical standby. Should the crippling attacks of vertigo continue, resort is had to operation, which in this country usually consists in destroying the labyrinth—and thus also the hearing on the affected side.

To the late E. R. Garnett Passe the paroxysmal nature of the attacks suggested a temporary disorder, which he thought might be a neurovascular disturbance, possibly arising from "underlying autonomic imbalance." Portmann and Despons[3] had reported hyperexcitability of the labyrinth after administration of drugs stimulating the sympathetic nervous system. Passe himself had observed gross dilatation of the vessels of the membranous semicircular canal during the fenestration operation, as a result of procaine block of the stellate ganglion. So, he reasoned, the labyrinthine vessels may go into spasm, and this may cause hyperexcitability; and the spasm might be relieved by interrupting the sympathetic pathways to the head and neck.[4] In a paper published posthumously Passe[5] reported that if stellate-ganglion block with 1% procaine subdued the tinnitus and improved hearing by air conduction, the patient was regarded as suitable for operation. In a first group of 45 patients the postganglionic fibres were interrupted by resecting the stellate ganglion; while a second group of 46 patients underwent preganglionic section. In the five years after operation over 60% of the patients in each group were completely relieved of their vertigo; and the condition of 33% was improved. These results have not been reproduced by other workers; and one wonders whether the Horner's syndrome which inevitably develops in patients who have had the stellate ganglion resected is not an even greater price to pay than the destruction of what little hearing may remain by the time that destruction of the labyrinth is undertaken. On the other hand, in the difficult cases of bilateral Ménière's disease, destruction of both labyrinths is to be avoided at almost any cost.

Rosen,[6] of New York, claims to have shown "for the first time since Ménière that the internal ear is not the exclusive seat of Ménière's disease." He had earlier reported that electrical stimulation of the chorda-tympani nerve under local anæsthesia produced auditory impressions of hissing, buzzing, roaring, or ringing, and that such stimulation sometimes gave rise to severe rotatory vertigo. He had also described the effects of sectioning the chorda tympani, alone or together with the tympanic branch of the glossopharyngeal nerve,

1. Ménière, P. *Gaz. méd. Paris*, 1861, **16**, 597.
2. Hallpike, C. S., Cairns, H. *J. Laryng.* 1938, **53**, 625.
3. Portmann, G., Despons, J. *Rev. Laryng., Paris*, 1928, **49**, 1.
4. See *Lancet*, 1951, i, 783. Mitchell, G. A. G. *Ibid*, p. 909. Passe, E. R. G. *Ibid*, p. 1280.
5. Passe, E. R. G. *Arch. Otolaryngol., Chicago*, 1953, **3**, 257.
6. Rosen, S. *N.Y. St. J. Med.* 1953, **53**, 1095.

in 14 cases of Ménière's disease; in 11 the attacks of vertigo ceased. These results, he claimed, led to the "inescapable inference that the internal ear is not the sole . . . portion of the nervous system from which the symptoms of Ménière's disease derive [and] that these symptoms may be mediated by way of sonic and equilibratory afferent fibres in the chorda tympani." Rosen now describes 2 cases of what he believes to be Ménière's disease, both unilateral and both with dead labyrinths on the affected side. The persistence of "Ménière attacks" despite a dead labyrinth he takes to be further evidence of some extralabyrinthine pathway by which symptoms are produced. In both cases the vertigo ceased after section of the chorda tympani. Of these 2 patients, 1 had had a fractured skull, after which "there was total absence of caloric response and total loss of hearing" on the affected side; in the other case the symptoms developed after mumps. Both fracture of the skull and mumps are recognised causes of unilateral perceptive deafness.

Fowler and Zeckel [7] pursue the search at a higher level. They declare that "certain personality types tend to develop tinnitus and perhaps vertigo under stress." The attacks, they find, are associated with certain types of life stress, including personal antagonism, sexual abstinence in the male, sexual conflicts in the female, and death of a near relative. Fowler and Zeckel do not, however, give convincing evidence of Ménière's disease in the 23 cases on which their report is based. In those cases where the deafness is described in detail, it is said to have been for low tones; whereas in Ménière's disease the loss is for high tones.

It cannot be said that great strides have been made in the attack on this troublesome disorder.

HALLUX VALGUS

CORRESPONDENTS, commenting on a leading article,[8] have expressed the view that the badly shaped shoe is the main cause of hallux valgus. This is not the only cause—even in some peoples habitually going barefoot hallux valgus is not uncommon [9]—but the evidence that shoes force the toes out of line is difficult to refute, and their deforming action is almost certainly the major ætiological factor in most cases of hallux valgus.

If we accept this, what are we going to do about it? There has long been a tendency to reverse the Victorian custom by which the foot had to fit the shoe rather than the shoe the foot. Knowles [10] describes an instance of an adult with mild hallux valgus who for three and a half years wore shoes, made on a special last, which were basically triangular and had a perfectly straight inner border. Foot symptoms were immediately relieved, and the degree of hallux valgus was materially lessened. In this country Mr. Pratt [11] has been pressing for the introduction of shoes with a straight inner border.

Shoes with a truly straight inner border are difficult to obtain; but some makers [12] specialise in shoes with fairly stringent inner borders. There would be, of course, no difficulty in producing such shoes if the necessary lasts existed. The trade, through the knowledge gained by the British Boot, Shoe, and Allied Trades Research Association, is well aware of the physiological need for these shoes. But two things militate against such a change. First, it would be very expensive to change every last; secondly, few people—and hardly any women—would buy the new shoes. The pioneer manufacturer of this type of shoe will meet a small demand from the highly foot-conscious; but unless the change is introduced simultaneously throughout the civilised world, with the support of massive publicity, we see no prospect of the demand increasing. It is not that the new shape of shoe would be intrinsically ugly; in such matters it is simply a matter of what one is used to (vide men's hats). The change could, we suppose, be introduced step by step if the trade and their designers agreed that they would gradually make shoes with straighter and straighter inner sides. But what stimulus is there for them to follow this costly course, so much against their immediate interests? There is only one rapid solution. At the command of a Schiaparelli or a Christian Dior waistlines rise or fall. Cannot a shoe designer be groomed to similar stardom? Of course the trade for its part may be waiting for a lead from the medical profession; but what form should this lead take?

7. Fowler, E. P. jun., Zeckel, A. *Psychosom. Med.* 1953, **15**, 127.
8. *Lancet*, Feb. 14, 1953, p. 331.
9. Kalcev, B. *Ibid*, 1952, ii, 937.
10. Knowles, F. W. *Med. J. Aust.* April 25, 1953, p. 579.
11. Pratt, C. A. *Lancet*, April 11, 1953, p. 746.
12. For example, Messrs. Hardy and Son, 6, Baker Street, London, W.1. See *Lancet*, May 9, 1953, p. 956.

SPONTANEOUS PNEUMOTHORAX

IN the early 19th century when Itard [1] first used the word "pneumothorax" and Laennec published his excellent description of the condition,[2] the qualification "spontaneous" was not used. Subsequently—for instance, in Powell's textbook of 1893 [3]—this qualification was applied to pneumothoraces where no cause could be found, as opposed to those associated with pulmonary tuberculosis or other disease. But when the production of a pneumothorax became a therapeutic procedure, all other varieties, except traumatic, were grouped as "spontaneous," since they arise through natural processes. Unfortunately, the group name is now commonly used for a single subgroup. Thus, a recent report by DuBose and others,[4] although entitled "Spontaneous pneumothorax: medical and surgical management," deals only with pneumothoraces unassociated with active pulmonary inflammation or neoplasm.

Laennec knew that air could be present in the pleural cavity without any perceptible change of structure of the pleura; and it was later recognised that a pneumothorax could occur in apparently healthy people.[5] In 1932 Kjaergaard [6] defined the condition as one in which there is a pneumothorax "without demonstrable cause in healthy individuals . . . in whom the lesion is not accompanied by fever or by [a clinically recognisable] pleural effusion." He called this "pneumothorax simplex"; others have named it "benign" or "idiopathic." Kjaergaard's definition is no longer adhered to, and the term is now applied even to cases where a cause for the air leak has been found. For instance, Brock [7] described "recurrent and chronic spontaneous pneumothorax" in 71 patients where a probable cause was discovered in all but 6; there were 25 with generalised or bullous emphysema, 11 with solitary or multiple cysts, 15 with small apical bullæ, and others with apical scars, pleural tears, or minute subpleural air-bubbles. DuBose and others found radiographic evidence of bullous emphysema in 57 of their 73 patients. This is a surprisingly high proportion, even in a series of patients ill enough to be admitted to hospital; the frequency of radiographically detectable pulmonary abnormalities in all cases of simple pneumothorax is probably very much less. As the majority have only one mild attack, which does not warrant extensive radiographic or thoracoscopic investigation, a cause will be found in only a few; and thus most cases will still fall within Kjaergaard's definition. But if a lesion seems with reasonable probability to have caused the pneumothorax, it would seem worth while removing the case from the category of simple spontaneous pneumothorax and classifying it according to the cause.

1. Itard, J. M. G. Dissertation. Paris, 1803.
2. Laennec, R. T. H. De l'Auscultation médiate. Paris, 1819.
3. Powell, R. D. On Diseases of the Lungs and Pleuræ. London, 1893.
4. DuBose, H. M., Price, H. J., Guilfoil, P. H. *New Engl. J. Med.* 1953, **248**, 752.
5. West, S. *Brit. med. J.* 1887, ii, 393.
6. Kjaergaard, H. *Acta. med. scand.* 1932, **77**, suppl. 43.
7. Brock, R. C. *Thorax*, 1948, **3**, 88.

Special Articles

RESULTS OF A QUESTIONNAIRE CONCERNING CONTROLLED HYPOTENSION IN ANÆSTHESIA

L. JENNINGS HAMPTON
M.D. Pennsylvania
DIRECTOR OF ANESTHESIOLOGY, YALE UNIVERSITY SCHOOL OF MEDICINE

DAVID M. LITTLE, JUN.
M.D., Harvard
ASSISTANT CLINICAL PROFESSOR OF ANESTHESIOLOGY, YALE UNIVERSITY SCHOOL OF MEDICINE

DURING the past few years the problem of excessive bleeding during surgical operations has been the subject of numerous investigations. The problem is scarcely new, and for many years surgeons and anæsthetists have found a solution in the use of chloroform anæsthesia, high spinal analgesia, or the meticulous posturing of the patient so that the operation site might remain superior. Gardner (1946) introduced arteriotomy by which blood was withdrawn from the patient preoperatively and later was partly or completely replaced in the same manner at the end of the operation, or even during the operation if necessary. Such preoperative reduction of the amount of circulating blood lowers the blood-pressure and causes peripheral vasoconstriction; and, when it is combined with the proper positioning of the patient, the net result is the reduction of bleeding at the site of operation. A more physiological approach was total sympathetic block (Griffiths and Gillies 1948). In this method the blood-pressure is reduced by spinal anæsthesia to achieve paralysis of the entire efferent sympathetic outflow. Gillies (1952) has stated that this technique is without doubt "physiological trespass" but has assumed that the arteriolar dilatation guarantees normal oxygenation of the tissue cells, and that the decreased cardiac output inherent in the technique is compensated for by the decreased peripheral resistance and therefore the decreased work of the heart. Proper posturing of the patient is again an essential feature of the control of bleeding, as it is in all methods of "controlled hypotension." The introduction of the methonium compounds (Barlow and Ing 1948, Paton and Zaimis 1948) provided a simple method of ganglionic blockade merely by injection, and led to the widespread use of induced hypotension for the control of excessive vascular bleeding in the field of operation, again in combination with proper positioning of the patient (Davison 1950, Enderby 1950).

AIMS AND EXTENT OF QUESTIONNAIRE

These techniques of induced hypotension for the control of excessive bleeding and the production of a relatively bloodless operation site have become increasingly popular among both surgeons and anæsthetists in the British Isles. Only within the last year or so has the method been used to any great extent on the American continent. Within this same period alarming warnings have been sounded, for it appears that certain complications of the technique have been much more common than were previously supposed (*Anæsthesia* 1952, Davison 1952, *Lancet* 1952). Knowledge both of these disasters and of the beneficial effects possible for a given patient are essential to the proper assessment of the technique and a true estimate of its position in anæsthesia and surgery.

Since the experiences of the anæsthetists in the British Isles with the technique of "controlled hypotension" greatly exceeds that of the anæsthetists on the American continent, questionnaires were sent to 602 members of the Association of Anæsthetists of Great Britain and Ireland in an attempt to obtain utterly anonymous, but unbiased, reports of the results of the technique, most particularly those fatal and non-fatal complications that might have been observed in its use. In the belief that the results of this questionnaire might be of some interest to those from whom the results originated, and with a feeling of deep gratitude toward those physicians of integrity who took part in this investigation, we submit this report.

Of the 602 questionnaires sent, 289 have been completed and returned up to now. This constitutes a return of 48%. The questionnaire was poorly worded, in certain instances; hence many of the figures are only approximate, and some editorial corrections became mandatory. For these reasons no statistical significance can be attributed to the results. These results do, however, indicate that "controlled hypotension" has been widely used, that complications have followed its use, and that deaths have been associated with, if indeed not due to, the technique.

RESULTS OF QUESTIONNAIRE

Each question from the questionnaire is printed below in its original wording, together with the results derived from an analysis of the 289 returned questionnaires:

(1) *Have you employed "controlled hypotension" to secure a bloodless operating field during surgical interventions?*

Yes	170
No	111
Yes, but have abandoned technique	8

(2) *What technique have you employed to obtain "controlled hypotension"?*

Arteriotomy	5
Spinal	51
Methonium compounds	166
Others (please state):	
Posture, plus deep ether or Pentothal	11
Veratrum viride	1
Chloroform	5
Amyl nitrite	1
Extradural block	7
Intercostal and sympathetic blocks	1
Local injection with adrenaline	2
Pronestyl with methonium compounds	1
Venesection	1
Various vasodilator agents	1
Barbiturates and Pentothal	1
Pethidine	1

Some anæsthetists used more than one technique.

(3) *In approximately how many cases have you used the technique?*

Arteriotomy	206
Spinal	6922
Methonium compounds	11,979
Others	2018
Total cases	21,125

(4) *What level of blood-pressure do you strive to attain?*

	Anæsthetists	*No. of cases*
60 mm. Hg or less	44	4571
60–80 mm. Hg	54	6847
70–80 mm. Hg	50	5727
80–90 mm. Hg	17	1392
90 mm. Hg	4	666
100 mm. Hg	3	232
Not stated	6	1690

(5) *Do you employ posture as a factor in obtaining a bloodless field?*

Yes	152
No	9
Sometimes	17

(6) *Do you employ vasopressor agents to return the blood-pressure toward normal?*

Yes	38
No	50
Sometimes	90

(7) *What contra-indications do you consider exist to the use of the technique of "controlled hypotension"? Please state:*

Cardiovascular disease in general, or any thrombosis	48
Cerebrovascular disease	32
Coronary disease	62
Arteriosclerosis	51
Cardiac disease, valvular disease, angina pectoris, myocardial infarction, decompensation	46
Hypertension	43
Renal disease	48
Hepatic disease	8
Too old: more than 40–50 years	51
Too young: less than 16–20 years	30
Anæmia	18
Hæmorrhage, preoperative	10
Shock	18
Hypotension	22
Poor physical condition, dehydration, low blood volume, chloride loss, &c.	30
Type of surgery: "luxury," minor, &c.	55
Difficult posture required: non-Trendelenburg, steep Trendelenburg, lithotomy	9
Dangerous, inexperienced, slow, or old-fashioned surgeon	4
Inexperienced anæsthetists or difficulties in anæsthesia	14
Poor operating-room or postoperative facilities	6
Pulmonary disease	4
Neurological disease	2
Diabetes mellitus	4
Miscellaneous—obesity, pregnancy, acute toxic disease, &c.	15

(8) *Have you encountered any of the following complications? If so, please check opposite the complication, and state the number of times that each complication has arisen:*

Anuria	54
Oliguria	30
Cerebral thrombosis	20
Retinal thrombosis	2
Coronary thrombosis	15
Mesenteric thrombosis	0
Reactionary hæmorrhage	164
Delayed postoperative recovery	190
Difficulty with vision	126
Others (please state):	
Cardiovascular collapse	6
Cardiac arrest	6
Auricular fibrillation	1
Ventricular fibrillation	1
Sudden blood-pressure drop	5
Pulmonary embolism	1
Air embolism	1
Hypoglycæmia in diabetes	2
Persistent hypotension	3
Ileus	1
Paralysis of bladder	1
Casts in urine	3
Spinal arachnoiditis	1
Vague cerebral anoxic states	3
Postoperative mental confusion	3
Postoperative lassitude	4
Prolonged drowsiness	3
Painful back and legs due to position	7
Total	553

(1 in 38 cases)

(9) *Have you encountered mortalities with the use of the technique of "controlled hypotension"?*

Yes	37
No	130
No, but have knowledge of deaths	11

If "Yes," please state the number of cases and the presumptive causes of death:

Renal failure	8
Cerebral thrombosis or cerebral anoxia	11
Coronary thrombosis	7
Cardiac arrest or failure	6
Reactionary hæmorrhage	2
Mismanagement (high spinal)	2
Over-heparinisation (arteriotomy)	1
Sudden death, cause unspecified	1
Death, cause not stated	1
Miscellaneous (4 probably unrelated)	7
Total	46

(1 in 459 cases)

SUMMARY

Questionnaires were sent to 602 members of the Association of Anæsthetists of Great Britain and Ireland concerning the use of "controlled hypotension" in anæsthesia. Of these questionnaires 289 (48%) were completed and returned, 178 anæsthetists reporting the use of the technique in more than 21,000 cases.

The results of this questionnaire should by no means be construed as an indictment of "controlled hypotension." When wisely used, in the carefully selected case, for an urgent and rational indication, the technique may prove most beneficial for a given patient.

However, a mortality-rate of more than 1 in 500 indicates that this technique is potentially dangerous, and it should therefore never be used in the absence of a specific and urgent indication or for the convenience of surgery. Obviously, it must never be used by the unwary, the unknowing, or the unskilled. Further, it is specifically contra-indicated in certain conditions; these contra-indications must be respected.

"Controlled hypotension" is indeed "physiological trespass"—the anæsthetist can never afford to forget this fact.

We are indebted to Dr. Georgina Y. Goodwin, resident in anesthesiology, for invaluable assistance in the tabulation of the figures.

REFERENCES

Anæsthesia (1952) **7**, 65.
Barlow, R. B., Ing, H. R. (1948) *Nature, Lond.* **161**, 718.
Davison, M. H. A. (1950) *Lancet*, i, 252.
— (1952) *Anæsthesia*, **7**, 116.
Enderby, G. E. H. (1950) *Lancet*, i, 1145.
Gardner, W. J. (1946) *J. Amer. med. Ass.* **132**, 572.
Gillies, J. (1952) *Proc. R. Soc. Med.* **45**, 1.
Griffiths, H. W. C., Gillies, J. (1948) *Anæsthesia*, **3**, 134.
Lancet (1952) Leading article, ii, 25.
Paton, W. D. M., Zaimis, E. J. (1948) *Nature, Lond.* **161**, 718.

THE PRACTITIONER IN THE N.H.S.

The Minister's Appeal

ADDRESSING the Annual Conference of Local Medical Committees, held in London on June 17, Mr. IAIN MACLEOD, the Minister of Health, said that when Sir Stafford Cripps in 1950 found it necessary to impose a ceiling on expenditure on the National Health Service, it became obvious that, with costs of all kinds tending to rise, we should sooner or later be forced into the position of selecting priorities. This was a problem that went wider than the health service.

"I made a rough calculation a week or two ago which told me that I could justify to the House of Commons and to the country, if medical need alone were the criterion, a capital programme of something like £1000 million, taking no account of the many hundreds of millions of pounds on maintenance expenditure that would involve in other years. But so, of course, could the Minister of Education in her field; so could the Home Secretary with all our needs for new prisons and institutions to replace some of our outmoded buildings; so could the Minister of Housing and Local Government and the Minister of Transport for the roads and so on."

If too much was spent in any particular field there would be all the less available for the more essential services.

THE DRUG BILL

Were we getting full value for the £40 million spent on prescriptions by general practitioners? (Taking into account the whole range of drugs, medicines, and appliances the figure was more like £60 million.) Partly because of fog, flood, and influenza, it had been very

difficult in the past year to get a true picture of how this expenditure was going; but the drug bill had climbed from £31½ million in 1949–50 to an estimated figure of £46½ million in 1953–54. There had been a steady increase in the total number of prescriptions dispensed; and a rise in their average cost from 2*s*. 9*d*. in the first year to 4*s*. 2*d*. now. Much of the rise in cost was due to the introduction of new and valuable, though expensive, drugs; and there had been a rise in ingredient prices until this year, although, again, it was only fair to say that some of the most important drugs, especially the antibiotics, had fallen substantially in price.

Under National Health Insurance in 1947–48, 7% of prescriptions dispensed were proprietary; in 1949–50 the figure rose to 15%; in 1950 to 18%; in 1951 to 23%; and in 1952 to 26%. There was no sign of a reversal of that tendency. The 1952 figure of 26% represented 52% of the ingredient cost and 44½% of the total cost. Everyone knew of examples in this particular field. The attention of the country—and of practitioners through *Prescribers' Notes*—had been drawn to a proprietary slimming preparation which if prescribed by its standard name would have produced a saving of £242,000 in 1951. The right way to look on that potential saving of nearly a quarter of a million pounds was to think what could have been done with the money.

"If that quarter of a million has gone—I don't suggest wholly—but partly unnecessarily, then it means that some hospitals have gone short and that I have not been able to authorise, as I would like to have done, certain improvements in many of the parts of the service that you all know need improving."

There were proprietary tablets which had as their main ingredients aspirin, phenacetin, and codeine which cost 6*s*. 3½*d*. for 50, whereas the same number of tablets of the comparable standard preparation cost 2*s*. 11*d*. A review in the *British Medical Journal* showed that certain asthma inhalant preparations cost four or six times the standard equivalent, "and you have been told, not by the Ministry, but by your own organisation, that there is little or nothing to choose in merit between them." It was true that many preparations had no exact official equivalent—that many preparations, particularly the antibiotics, were in fact only made up in proprietary forms. It was also true that a most important contribution to our exports—not less than £30 million in a year—was made by the pharmaceutical industry. It was, true, too, that they devoted a good deal of money to research, from at least some of which all the people in this country might well benefit. But this was not true of all preparations and it was not true of all firms.

"It is here then that, quite frankly, I want your help. I cannot tackle this wholly by myself, and I do not pretend that I can. You know the way in which doctors can help. I know perfectly well it is easier to say these things than to do them, but we can make careful use of the *National Formulary* preparations. We can by referring to the two tables of proprietary preparations in the formulary—which shows those for which an equivalent standard preparation is available—decide whether they are of substantially the same therapeutic effect as perhaps another preparation which could be prescribed. I think it is important to stress here that while many formulary preparations are cheaper, there is no reason to regard them, as I am sure you do not on that account, as being inferior. They were recommended by medical and pharmaceutical experts quite independently of my Ministry; they conform, as you know, to the standards laid down in the *British Pharmacopœia* or the *B.P.C.* Again, I think you can help by satisfying yourselves, before prescribing a proprietary preparation that is not included in the two formulary lists, that there are adequate grounds for believing that its therapeutic value is superior; and finally—and again this is easier no doubt to say than to do—by resisting pressure from patients to prescribe particular preparations which they have had recommended to them or about which they have read in technical or semi-technical or lay papers."

"You all receive copies of the *Prescribers' Notes* and I intend to issue to you a price-list of preparations and proprietary preparations listed in the formulary which are frequently prescribed. We have had a clear lead from Sir Henry Cohen's committee, and when the official classification of proprietary preparations has been completed, which will be in a very short time, I propose to circulate this to you all. Finally, as I told the House of Commons, I must myself by cost investigations satisfy myself that the prices being charged are themselves not excessive. In my desire to help there I am setting on foot as many investigations as I can undertake into selected preparations in the categories which Sir Henry Cohen's committee advise me should be prescribable provided a satisfactory price agreement can be reached."

Nothing whatever in what he had said, or in what he intended, infringed in any way on the doctor's right to prescribe.

HOSPITAL AND GENERAL PRACTITIONER

Among the things that we wanted to achieve, said the Minister, was that more patients were treated in their own homes and on the whole fewer in hospital.

"I do not put that forward on economic grounds, although that is certainly a factor, because hospital treatment works out at £700 a year, whereas domiciliary treatment is a quarter or less of that figure. But many patients would, in fact, benefit greatly if they could be treated in their own familiar surroundings without the disturbance and stress and anxiety of removal to a hospital. If the cost of the hospital service continues to grow, as it shows every sign of doing, it is inevitably going to absorb more and more of the money that can be set aside for the health service. So we must try, if we can, to lighten the load on the hospitals provided that can be done without any detriment to the patient."

The treatment of a greater variety of patients at home could add enormously to the value and interest of the work of the general practitioner. Mr. Macleod regarded direct consultation between consultant and practitioner as of the first importance, and he would like to see here and there more advantage taken by the practitioner of the opportunity of meeting the consultant in domiciliary consultation in the patient's home. It was also of first importance that the practitioner should have direct access, not of charity but of right, to the X-ray and pathological services.

"He should be told, too, and he should be told at once, when his patient leaves hospital; and when he refers a patient for consultation he should receive the considered opinion always of a senior member of the staff. Then he should always be made welcome in the hospital no matter whether he is accompanying a consultant on his rounds or visiting a patient or just dropping in—he should be part, in the fullest sense, of the hospital service in his particular area. Now this is common practice in many places, but there are many of you who know that this sort of welcome without jealousy is not always extended to the G.P. in every hospital."

As regards the liaison between the practitioner and the local health authority, particularly in preventive work, he had been struck by the differences apparent in different areas. In some places—usually where there was an able and energetic medical officer of health—there was the closest contact between health visitors and practitioners, but in others the partnership should be closer. Many people felt that too many cooks were concerned with the welfare of the patient, and feared that the practitioner might be crowded out; but there was no danger of that provided he was recognised to be the clinical head of the whole team—"the clinical leader of all the domiciliary health services, bewildering as they may be in their variety, which are provided for people in their homes."

SOLVING THE PROBLEMS

We were engaged in a magnificent experiment in social medicine, said Mr. Macleod, and it must not be strangled by too much administration or central direction. Only

because the necessities of the financial position at the moment forced him to do so did he keep the reins firmly in his hands. All his instincts were towards giving greater and greater freedom to those who really worked the health service, and everything he did would be directed to that end however crabwise his movements appeared to be.

"I don't assume, when proposals are put to me by the medical, dental, or nursing profession that they are necessarily biased or necessarily wrong. On the other hand, I don't work on the assumption that you are necessarily right either. But I would like to say this. I want now, as I have always done since I became Minister, to seek your help and the help of all the other professions in the National Health Service. This is not . . . a job that the Minister can do alone, or the department alone, nor the doctors, or any of the other professions. It is essentially a matter in which we must work together; it is essentially something in which I need your help, and I am very ready to come to you for advice. Any help I can give is at your disposal, but it is only in partnership together that we are going to solve these problems and achieve the true potentiality of our National Health Service."

DR. TALBOT ROGERS, chairman of the General Medical Services Committee, in thanking the Minister for his address, referred to discussions with the Ministry during the past few years on the mounting cost of the drug bill. The committee, he said, would do all it could to assist in stabilising the cost of the pharmaceutical service provided this was not incompatible with the essential needs of the patient.

Public Health

AN EXPLOSIVE OUTBREAK OF FOOD-POISONING CAUSED BY SALMONELLA DUBLIN

A. M. McCALL
M.R.C.S., D.P.H.
MEDICAL OFFICER, CHARD BOROUGH AND RURAL DISTRICTS, SOMERSET

ON Sept. 25, 1952, an outbreak of food-poisoning caused by *Salmonella dublin* affected a large number of children in schools in Chard and the surrounding rural districts, and also a smaller number of adults mainly resident in the borough of Chard. The outbreak was brought to my notice soon after the schools had assembled on Friday, Sept. 26. As school-children were involved, a rapid analysis of a large number of cases was possible, and evidence pointed strongly to milk as the most likely vehicle of infection. The milk to the school originated on a farm supplying tuberculin-tested (T.T.) milk, most of which was consumed at this and other schools, the remainder being delivered to the public. On investigation of the herd concerned it was found that one cow had been taken ill and isolated on Sept. 23. Within twenty-four hours of the start of investigation *S. dublin* had been isolated from milk from the cow and from fæces of 2 of the victims.

NOTIFICATION

On the morning of Sept. 26 the acting head teacher of a large school in Chard found that about 100 children were absent and several in school were complaining of sickness and diarrhœa. He immediately telephoned the health department.

All the general practitioners working in the area were at once informed of the outbreak and asked to send any specimens of vomit and/or fæces to the Public Health Laboratory as soon as possible. The director of the laboratory was also informed.

Only 1 notification was received from a general practitioner. Some practitioners, however, sent specimens to the Public Health Laboratory, and copies of the reports on these were sent to the health department.

METHOD OF INVESTIGATION

The first information came from a secondary modern school. Many of the children came from outlying villages and the head teacher was asked to make a list of absentees and their addresses, and to state whether they took school meals and/or school milk, or neither. Other schools which could be approached on the telephone were asked to do likewise. These lists were collected, and a rapid analysis pointed towards school milk; but it was found later that there were some cases of illness among children and teachers who had neither milk nor meals in school and some who had meals only.

All the schools approached received their milk from the same source. The supply was known to be T.T. non-pasteurised milk, and the bottling and retail department of the suppliers was next visited. The routine was for the bulk supply from the herd for the day—i.e., morning and evening milk—to arrive in the bottling department in the late afternoon, when it was bottled and put in the refrigerator overnight. The milk was sent out at 7.30 next morning. The bottling machinery and refrigerator were all in good order, the methods of cleaning and sterilisation were satisfactory, and no member of the staff had been ill or had any symptoms of disease. Of the 150 gallons of T.T. milk being handled daily 90 gallons went to schools.

Fortunately all the milk came from one herd, and the farm was next visited. The farm building and milking stalls were of modern type with a good water-supply and concrete yards which were all in good condition. Electrical milking apparatus was used. The cows being milked were in good health, but it was discovered that one cow (Ladybird) had been isolated with mastitis on Sept. 23. She was isolated about 11 A.M.; therefore it was possible that milk from her in the morning had got into the bulk supply distributed on Sept. 24. A sample of her milk was taken and, together with a bottle thought to be left over from Sept. 24, sent to the Public Health Laboratory. The veterinary surgeon looking after Ladybird was informed of the outbreak. He immediately examined her and expressed the opinion that she now presented a picture of a salmonella infection. Immediate arrangements were made for all further milk from this farm to be heat-treated, and general practitioners were informed that a salmonella was a very likely cause of the outbreak. This part of the investigation was completed by midday.

By next morning the laboratory had isolated *S. dublin* from the cow's milk and from the fæces of 2 patients. The general practitioners were informed of this result and of the sensitivity of this strain of *S. dublin* to chloramphenicol. All the affected schools were informed of the cause of the outbreak and warned of the danger of secondarily infected cases. The need for strict personal hygiene and extra cleaning of all cloakrooms was emphasised.

SYMPTOMS

The order in which the symptoms presented varied. All the patients had nausea, often but not always followed by vomiting. The patients who did not vomit appeared to have severe abdominal pain, but so did many who also vomited. A fairly common symptom in the early stages was severe headache, mainly frontal, with some giddiness. This type of headache has been noted previously, and *S. dublin* has been found to be the causal organism of meningitis (Guthrie and Montgomery 1939). Extreme pallor was a striking sign. Temperatures varied from 99·5°F to as high as 105°F, but most were 100°–102°F. The length of illness varied, but most of the patients recovered in three or four days. There were no deaths.

INCUBATION

Incubation varied from four to forty-eight hours, but most of the patients were affected from twenty-four to thirty hours after taking the milk.

DISTRIBUTION

The accompanying table shows the schools affected; 598 children were affected and 1256 school days lost.

DISTRIBUTION OF CASES

School	No. on roll	No. of children taking milk	No. of children ill	No. of school days lost	No. of adults affected
Buckland St. Mary ..	43	42	28	90	—
Chaffcombe	32	32	11	31	—
Chard Infants ..	135	134	43	75½	—
Chard Junior	304	240	127	243	—
Chard Grammar (Boys)	118	118	34	53	2
Chard Secondary Modern	357	135	95	229	3
Combe St. Nicholas ..	71	50	43	72	—
Otterford	26	26	14	14½	—
St. Gilda's Convent ..	210	192	82	195	3
Tatworth	99	91	84	188	1
Wambrook	17	14	14	29½	—
Whitestaunton	24	22	16	35½	—
School total	1436	1094	591	1256	9
Other notifications ..	..	..	7	10	3

Some children affected did not take school milk. This is explained in two ways.

(1) On Sept. 24 the schools receiving midday meals from the central school kitchen had rice pudding. Although this was made from satisfactory milk it was stodgy, and in some cases the school milk was used to make it more palatable.

(2) Some children who did not drink the school milk came from homes supplied from the same source. They were infected in common with other members of their family.

The adults were affected in one of these two ways.

No obvious difference in susceptibility was noticed, and there was no sex difference. The fact that fewer older children were ill is explained by the fact that, whereas the percentage of milk drinkers is about 90 among young children, it is only about 50 in older children. The small number of adults is explained by the fact that few went to the doctors for treatment, and therefore the exact number is unknown. Less milk was distributed to the public than to the schools. No doubt also most adults take their milk in some hot beverage, such as tea, and the bacterium is often destroyed in this heating.

BACTERIOLOGY

All of the 7 specimens of fæces obtained from persons with symptoms of food-poisoning contained *S. dublin*. The Salmonella Reference Laboratory confirmed the identification.

S. dublin having been isolated from Ladybird's milk, it was important to discover how she had become infected. She had calved four or five days before becoming ill, and her calf had been put on the herd nursing cow. First, the farm hands were examined, and samples of their fæces were sent to the laboratory; all were negative. It was discovered that one of the milkers (A.B.), who was on holiday during the week of the outbreak, had been infected in a smaller outbreak due to the same organism on an adjacent farm in 1947. He had assisted at Ladybird's calving, and this was regarded as highly suspicious. However, repeated specimens of his fæces proved negative. The report on his blood was as follows:

S. typhi	(O)	1/80 + 1/160 trace
S. paratyphi-B	(O)	Less than 1/40
S. paratyphi-B	(H)	" "
S. enteritidis	(H)	1/40 " "

S. dublin shares the (O) antigen of *S. typhi* and the greater part of the (H) antigen of *S. enteritidis*. The paratyphoid antigens were used as controls. The results suggested an old rather than a recent infection, in agreement with his history. His medical practitioner states from his records that A.B. had had pyrexia of unknown origin in September, 1950, and had been off work for thirteen days; he then had headache and abdominal pain and was treated with penicillin. He did not respond, but his temperature subsided slowly, after being about 100°F for five days. Infected persons have been known to carry *S. dublin* for twenty-one months (Harhoff 1941), but nobody for five years. In spite of the rarity of carriers of salmonella and the negative findings, A.B. must remain under suspicion.

As the milk from an adjacent farm had been the cause of a smaller outbreak due to the same organism in 1947, it was considered that there might be a link between the two farms, possibly a common contaminated water-supply. Moore swabs (Moore 1948) were inserted in the water-supplies to both farms, and in all streams and drains nearby. None of the swabs were positive.

As Ladybird's fæces were positive, it was suggested that the milk had been contaminated in handling. She was slaughtered, and her udder was removed and opened aseptically, samples of milk were pipetted off from each quarter, and *S. dublin* was recovered from the milk. Her liver was enlarged and pale and showed signs of fatty degeneration; but it was not sent to the laboratory. Clarenburg and Vink (1947) have found that, when other organs are affected, the liver always contains *S. dublin*.

The remainder of the herd were examined by the regional veterinary investigation centre of the Ministry of Agriculture and Fisheries. None of the samples of milk and fæces contained salmonella. No samples of blood were taken. Ladybird's calf, which had been on the mother for only two days before she became clinically ill, was found to have *S. dublin* in the fæces; it did not infect the nursing cow on whom it was put, and recovered after treament with sulphadimidine. On Oct. 2 a heifer developed symptoms of enteritis; it did not respond to treatment, and was slaughtered on Oct. 9. A cow was similarly affected on Oct. 11, and slaughtered on Oct. 14. On Nov. 5 a further cow was affected and was given treatment; she appeared to be healthy, but on Nov. 24 still had *S. dublin* in the fæces. She has not been allowed to return to the herd. It may be of significance that all the animals infected appeared to acquire the disease in a field which is used annually for the local agricultural show. The possibility of infection persisting at the site of the latrines was considered, but a few bacteriological examinations of the soil were unproductive. Another feature of this field may be of more importance: alone of all those in use on this farm it depends for drinking-water on a brook, the river Isle at Eleighwater, which rises some two miles away, near the farm which was the source of a small milkborne epidemic in 1947. Field (1948) has shown in West Wales that *S. dublin* infection of cattle is not uncommonly waterborne.

CARRIERS

In a boys' school, where 29 of the boarders were affected, samples of fæces were taken from them all on Sept. 29. They were all negative.

It was expected that secondary cases would follow due to healthy carriers. In an effort to detect these carriers Moore swabs were inserted in the main drains of all the schools before they entered the sewers or soakaway four weeks after the outbreak. Not one of these was positive.

The only person known to be still unfit at the end of November was a kitchen hand. Although specimens of her fæces were negative, she was still having abdominal discomfort and occasional severe diarrhœa. She finally returned to work symptom-free on Dec. 1, when her stools were still free from *S. dublin*.

EFFECT ON SCHOOLS

The most serious effects of the outbreak were felt by the school population, the work of the smaller schools being completely disrupted. The loss of 1256 school days in a term due to one outbreak is considerable. If children work a five-day week for forty weeks a year, this is equivalent to more than six years. In an epidemic of this size it would probably have been necessary to close the schools; but a weekend intervened, and by the following Monday the number of absentees was many fewer than when they had closed on the Friday.

PASTEURISATION

The opponents of pasteurisation always use as one of their strongest arguments that children will never drink "cooked milk." Of course, if there is a cooked taste about pasteurised milk the technique is at fault, and usually it is impossible for a normal person to detect whether milk is raw or pasteurised.

This outbreak occurred in a rural area and one of the most important milk-producing areas in the country. Most of the children came from villages and probably have as sensitive a palate as any, so far as milk is concerned. It is therefore interesting to see what effect the outbreak had on the school consumption of milk.

Before the outbreak 1094 of 1436 children were taking milk in the affected schools. Three months later 1030 of 1443 were taking milk. The weather then was considerably colder, and there is a slight seasonal falling off in the consumption of milk every year. Immediately after the outbreak there was a considerable drop in the numbers. However, they have slowly increased, and now are 64 less than previously. The fall in numbers has been greatest in the rural primary schools and the private girls' school. There has not been one complaint by the children against the heat-treated milk. The fall is entirely due to parents stating that they do not wish their children to take the milk. It was noted in this part of the investigation that the number of children taking milk in schools depends a great deal on the head teacher, particularly in the smaller schools.

DISCUSSION

In many previous outbreaks the milk has contained *S. dublin* owing to fæcal contamination, yet efforts to isolate it from the milk failed (Conybeare and Thornton 1938). No record has been found of any outbreak in which so many persons have been affected. Tulloch (1939) reported that, in 1926, 373 persons were affected by a milk-borne outbreak due to *S. dublin* in Dundee. The large number in the present outbreak may have been due to the fact that in this instance the cow was excreting *S. dublin* in considerable numbers and the milk was more heavily contaminated than might otherwise have been the case. The morning milk, which was the contaminated milk and was later bulked with the afternoon milking, was not refrigerated till evening, and in the meantime incubation could easily have taken place.

The original source of infection is still undiscovered. The fact that one milker was involved in two outbreaks in five years is interesting, but it must be remembered that *S. dublin* is the commonest found in bovines (Ritchie and Clayton 1951). However, if he were the cause, which has not been proved, he might well have infected the cow during calving. She was originally presented as a case of mastitis and only later developed bowel symptoms.

CONCLUSIONS

Notification.—This was a large outbreak which the health department was able to notify to the general practitioners. It would therefore be reasonable to expect 100% notification of cases treated; but this was far from being achieved. One is bound to assume that a large number of small outbreaks must occur which go unnotified or may be notified much too late for any useful investigation to be made. The health department was fortunate in this instance that the acting head teacher of a school reported to it immediately by telephone. The investigation could thus be brought to a satisfactory conclusion very much sooner than might otherwise have been possible.

School Milk and Meals.—In this area the medical officer of health is also the medical officer responsible for inspections in the schools. The source of the school food and milk was therefore known to him without investigation, and this again was an important factor in avoiding waste of time.

T.T. Milk.—The source of infection in this outbreak was T.T. raw milk. The fact that the milk-supply is tuberculin-tested leads to a false sense of security, as this outbreak has shown.

RECOMMENDATIONS

General practitioners should be asked to inform the health department whenever two or more similar cases of food-poisoning occur simultaneously, because only a small percentage of patients seek medical advice. The health department can then get in touch with other general practitioners, who may have like cases.

Where the medical officer of health is not the school medical officer it is a great advantage for him to be informed of the sources of milk and meals at all schools in his area as a routine.

Wherever possible, pasteurised milk should be supplied to schools, even if extra expense is incurred in so doing.

SUMMARY

An explosive outbreak of food-poisoning due to *Salmonella dublin* affecting 610 known cases in Somerset in 1952 is described. The food causing the outbreak was T.T. raw milk supplied to schools and the public.

S. dublin was isolated from the milk, udder, and fæces of the affected cow. It was also recovered from all samples of fæces from patients showing signs of illness.

When pasteurised milk was supplied the epidemic finished in a few days.

My thanks are due to Dr. J. A. Boycott, director of the Public Health Laboratory, Taunton, for laboratory work, for help and advice throughout the investigation, and for criticism of this report; to Mr. W. B. Martin, M.R.C.V.S., for help in the investigation of the herd; to the sanitary inspectors of the Chard Rural District Council, especially Mr. Eric Whisker, whose help was invaluable, particularly in the early stages of the inquiry; and to Mr. J. Handel, acting headmaster, whose prompt action in telephoning the health department had such an important bearing on the investigation.

REFERENCES

Clarenburg, A., Vink, H. H. (1947) *Tijdschr. Diergeneesk.* **72**, 711.
Conybeare, E. T., Thornton, L. H. D. (1938) *Rep. Minist. Hlth, Lond.* no. 82.
Field, H. I. (1948) *Vet. J.* **104**, 251, 294, 323.
Guthrie, K. J., Montgomery, G. L. (1939) *J. Path. Bact.* **49**, 393.
Harhoff, N. (1941) *Zbl. Bakt.* **147**, 194.
Moore, B. (1948) *Mon. Bull. Minist. Hlth Lab. Serv.* **7**, 241.
Ritchie, J. M., Clayton, N. M. (1951) *Ibid.* **10**, 272.
Tulloch, W. J. (1939) *J. Hyg., Camb.* **39**, 324.

Food-poisoning in Lancashire

The Minister of Health, answering a question in the House of Commons on June 18, said that 734 cases of food-poisoning had been notified in Preston and the surrounding district up to June 17. 15 patients were still in hospital, and there had been 1 death. The source of infection was meat pies, contaminated with a virulent form of salmonella. The manufacture of these pies had been stopped, and investigations were continuing to determine the way in which they had become infected. He was satisfied that all appropriate measures had been taken to control the outbreak, which now appeared to be at an end.

Dr. A. Dodd, medical officer of no. 3 division of the Lancashire county area, tells us that the food responsible was approximately 6000 meat pies manufactured in

a large bakery on June 10 and 11. Possibly, too, some pies baked on June 9 and 12 were infected.

A report on the morning of June 13 of 2 cases, and the information that meat pies, among other foods, had been eaten, resulted in a decision the same morning to stop production of meat pies. Staff concerned were interviewed and excluded from work when this was justified; and fæcal specimens were submitted for investigation. Steps were taken to get unsold meat pies destroyed or subjected to laboratory tests.

Salmonella bovis-morbificans was isolated from fæces of patients affected and from the meat pies, but not from the constituents (it has not been possible to obtain samples of meat from each source). Salmonella organisms were isolated from several persons employed at the bakery who were probably infected by eating meat pies, but the findings in one case may prove significant. Investigations continue, particularly concerning meat-supplies.

Clinically the incubation period has varied from 6 hours up to 30 hours—18 to 24 hours has been common. Shivering and colic or vomiting (sometimes very prominent) has been followed by diarrhœa accompanied by headaches, pains in the limbs, and general prostration. The illness has lasted for from 8 hours to 5 days. The severity of symptoms has been very variable. Primary cases are still being reported, and also a few secondary cases.

Up to last Monday the outbreak was thought to have involved over a thousand cases[1]; and a death in Lancaster on June 20 may have been due to the infection.[2]

Lining a Reservoir

A rubber bag holding 12,000,000 gallons of water is to be fitted into a reservoir at Easington, near Sunderland, which was cracking because of coal workings. After two years' experiments and tests, Sunderland and South Shields Water Company have accepted the Dunlop Rubber Company's plan for fixing 16,000 square yards of rubber to the reservoir with a ton of adhesive. The rubber bag will weigh 100 tons.

1. *Manchester Guardian*, June 23, 1953.
2. *Ibid*, June 22, 1953.

Parliament

QUESTION TIME

Negligence in a Military Hospital

Wing-Commander N. J. HULBERT asked the Secretary of State for War whether inquiries were now completed in regard to the death of Private Donald Harrison, of Stockport, who died in Moston Hall Military Hospital in April.—Mr. A. H. HEAD replied: Private Harrison, a young man aged 18, was called up for military service in January, 1953, when he was passed as medically fit. On March 13 at Wrexham he reported sick with a pain in his back which the medical officer in charge of his unit diagnosed as fibrositis. He again reported sick on March 26 when the medical officer diagnosed "Query hysteria" and ordered his admission on March 26 to the military hospital at Chester.

On admission he was given, by the admitting medical officer, a preliminary medical examination which included a detailed examination of the central nervous system for the purpose of allotting him to the appropriate medical division of the hospital. The admitting officer made a firm but not final diagnosis of hysteria. This preliminary examination was correct in so far as Harrison was undoubtedly suffering from hysteria. The fact that it was not discovered that he was also suffering from a rare and malignant disease was not necessarily at this stage due to negligence since a more detailed subsequent examination should have taken place after admission to the ward.

After admission Private Harrison was required by the medical staff of the hospital to fend for himself and other patients were forbidden to help him. The treatment of hysterical patients does require that they should be encouraged to help themselves but in no circumstances should it entail harshness. Although he complained that he could not use his legs, he was left to get about as best he could by himself. This treatment continued for five days during which time Harrison's condition deteriorated, and I am satisfied that the continuance of this type of treatment was due to negligence and undoubtedly resulted in harshness. A full physical examination is always required before a diagnosis of hysteria can be justified and should have been made on the first day in the ward. The medical specialist looking after Harrison should have satisfied himself that this had been done. This he neglected to do. Furthermore, although during these five days Harrison frequently complained of pain in his legs, thighs, and back, and although this was recorded by the subordinate nursing staff, the day sister in charge of the ward never drew the attention of the medical specialist to Harrison's repeated complaints.

This wrong and harsh treatment was continued despite the comments and protests of at least one other patient in the ward. It was not until March 31 that Harrison was seen by a psychiatrist and thereafter received sympathetic handling, but even at this stage a full examination had not been made. On the night of April 1 the medical orderly became worried about Harrison's condition and called the orderly medical officer, and then for the first time Harrison was given a full medical examination. The orderly medical officer realised at once that Harrison was dangerously ill, and from this time he was treated for the malignant disease from which he was suffering. Harrison died early on the morning of April 5. At the time of his admission to hospital Harrison's illness had undoubtedly reached a stage when death was inevitable since malignant disease of this type in youth, though rare, grows very rapidly. I do not suggest that this in any way excuses the mistakes made in the handling of this case.

After Harrison's death it should have been abundantly clear to the commanding officer of the hospital that serious irregularities and mistakes had occurred. Yet, as far as I can ascertain, no thorough inquiry was instituted by the commanding officer although on May 18 he stated that a full inquiry had already been made by himself and that he was satisfied that there was no truth in the allegations that there had been ill-treatment of patients.

I have been into the whole of this serious occurrence most carefully and I am convinced that it was caused not by any fault in the method of procedure laid down for Army hospitals but by the failure of certain individuals to carry out their duties. Members of the Army Medical Services carry heavy responsibilities and those who fail to discharge them must be called to account. The commanding officer will be called to account for his conduct in this matter and is to be tried by court-martial. The medical specialist concerned, who left the R.A.M.C. in May, will be reported to the General Medical Council. The day sister concerned, who is a civilian, has had her contract terminated and will be reported to the General Nursing Council.

I have written to the mother of Private Harrison expressing my extreme concern and disquiet about the way her son was treated, and I would like also to tell the House how much I regret this lamentable occurrence.

N.H.S. Specialists in Scotland

In answer to questions as to how many specialists were employed under the N.H.S. in Scotland Commander T. G. D. GALBRAITH gave the following figures:

Date	Consultants			S.H.M.O.s			Total Consultants and S.H.M.O.s		
	Whole-time	Part-time	Total	Whole-time	Part-time	Total	Whole-time	Part-time	Total
31.12.49	283 (*43·8%*)	363 (*56·2%*)	646	163 (*59·5%*)	111 (*41·5%*)	274	446 (*48·5%*)	474 (*51·5%*)	920
31.12.50	325 (*45·9%*)	383 (*54·1%*)	708	174 (*59·8%*)	117 (*40·2%*)	291	499 (*49·9%*)	500 (*50·1%*)	999
31.12.51	348 (*47·6%*)	383 (*52·4%*)	731	205 (*63·9%*)	116 (*36·1%*)	321	553 (*52·6%*)	499 (*47·4%*)	1052
31.12.52	372 (*49·6%*)	378 (*50·4%*)	750	219 (*66·4%*)	111 (*33·6%*)	330	591 (*54·7%*)	489 (*45·3%*)	1080
31. 3.53	368 (*49·2%*)	380 (*50·8%*)	748	224 (*67·3%*)	109 (*32·7%*)	333	592 (*54·8%*)	489 (*45·4%*)	1081

Tuberculosis in Glasgow

Mr. JOHN RANKIN asked the Minister the number of new cases of pulmonary tuberculosis notified in Glasgow in the first quarter of 1953, and how this compared with each quarter of 1952 and 1951.—Commander GALBRAITH replied: There were 622 notifications of pulmonary tuberculosis in the first quarter of 1953, a higher figure than in any of the quarters in 1951 or 1952 except the 644 in the second quarter of 1951.

Mr. RANKIN asked the Minister how many beds were available, per 100 new notifications, for the treatment of pulmonary tuberculosis in the whole of Scotland and in the area under the Western Regional Hospital Board.—Commander GALBRAITH replied: At the end of 1952, the ratio was about 82 beds per 100 notifications for Scotland as a whole, and about 77 beds per 100 notifications for the Western Region alone.

Nurses and Pencillin Sensitivity

Mr. ALFRED HARGREAVES asked the Minister of Health the number of district nurses who had developed a sensitivity to penicillin and could not undertake further nursing duties; and what special precautions were available to protect nurses exposed to this risk.—Mr. IAIN MACLEOD replied: The total number of district nurses affected is not known, but a special inquiry has shown that in 70 local health authority areas 73 nurses had become sensitive to penicillin, and had to give up nursing for varying periods. There is evidence that the incidence can be reduced by strict observance of technical precautions and I have at once obtained advice on this from my Standing Medical Advisory Committee. I am circulating this advice urgently to local health authorities and others concerned. Nurses who have to give up work by reason of sensitivity to antibiotics are entitled to the normal sick-leave allowances and may, in appropriate cases, qualify for incapacity benefit under the National Health Service (Superannuation) Regulations. They may also, when the circumstances warrant it, qualify for industrial injuries benefit. The numbers, if any, who may have to give up nursing permanently are not yet known.

Mr. HARGREAVES: Would the Minister consider approaching the employing authorities so that they may gain the requisite information from their nursing superintendents? Would he compare the means whereby penicillin is administered in hospitals where the incidence of this sensitivity is less, and possibly learn of a method by which this risk can be reduced for nurses who have to undertake the administering of a great deal of penicillin? Mr. MACLEOD: I will look carefully into what the hon. Member says. I know there is a great deal of truth in it. Perhaps I might send him a copy of the advice I have been given by the Medical Advisory Committee, which covers many of the points he raises.

Chalk Content of Flour

Dr. BARNETT STROSS asked the Minister of Food the total amount of chalk added to flour in any given year; and from what source the chalk was obtained.—Major GWILYM LLOYD GEORGE replied: In the twelve months ended May 23, 1953, 11,369 tons of calcium carbonate were added to National flour. The whole of the supplies conformed to the specifications of the *British Pharmacopœia* and were obtained from home sources.

Dr. STROSS: Is the Minister aware that a great deal of discussion is going on whether there is any need to add chalk to our flour today, and that the original views are suspect? Are the Ministry of Food doing anything to check up on this problem and see whether the use of this substance can be discontinued?—Major LLOYD GEORGE: The hon. member knows that unanimity very seldom exists on these points. This was the result of the Committee of 1941. The reason that it is still being maintained is because there is a proved deficiency of calcium intake in our diet. Dr. STROSS: Does not the Minister agree that recent experiments in South Africa have shown that the work in 1941 may well be not as accurate as we should like and may not justify the use of 11,000 tons of chalk in our flour every year? Will the Ministry of Food look at this question again? Major LLOYD GEORGE: I am always prepared to look at important matters of this sort, but it is admitted that there is a very serious shortage of calcium intake.

In England Now

A Running Commentary by Peripatetic Correspondents

ONE of my most cherished possessions, purchased regardless of cost—five shillings, to be exact, including frame—from a cottager patient of mine is a later version of the German picture *The Broad and Narrow Way* originally designed by Mrs. Charlotte Reihlen of Stuttgart in 1862 and painted for her by young Herr Schacher of that city.

Not much happens along the narrow way, which may be why it is attracting all too little custom. There is a chapel, a Sunday School, a deaconess institute; you may have a drink of water if you like and there is a loose lion to be negotiated, but after that it is all plain sailing or, rather, a short and gentle uphill stroll to a heaven of golden towers and minarets. How different is the broad way. Once through the inviting gate surmounted by "Welcome!" in large letters there is never a dull moment. Small wonder that most people go this way, some of them by car and one of them on a bicycle. Hardly are you inside before you are beckoned into a cottage by an attractive young woman. If you prefer alcohol there is to your left a pleasant outdoor café, and within a stone's throw not only a theatre, but also a ballroom flying a union jack and open on Sundays.

Beyond, with a loan office conveniently situated under the same roof, is a gambling house, from an upstairs window of which is suspended the corpse of a (presumably unsuccessful) gambler. On coming out of the loan office you may spend an amusing half-hour at the lottery table before going on past a couple of convicts to witness a pitched battle with a cavalry charge in progress backed by artillery and infantry (in that order). All the troops taking part are in full dress. Just this side of hell there is a Sunday train, and dominating all is what is apparently an optician's sign. Between heaven and hell there is a pretty solid looking rainbow.

* * *

One of the many responsibilities of the present-day householder is the execution of minor day-to-day repairs. A few weeks ago a disorder of function developed in an important piece of hydraulic machinery, and my own efforts at repair having resulted in the loss of what little remaining function there was, I was constrained to seek consultant advice from the local plumber. He and his assistant soon restored the contraption to working order and in due course their bill was dropped through my letter-box.

"Dr. to Wm. Bloggs & Bro.
To: taking down waste water preventor cistern, removing syphon box, making and fixing new copper clack, re-assembling and refixing .. .. £1 1s.

Reading this elegant document, my thoughts went back to those spacious days in the '30s when our paying patients provided us with both our bread-and-butter and our motor-cars and when everything from the removal of a wen to an abdomino-perineal resection was discreetly cloaked under the all-embracing term "For professional services." How much more satisfying for our patients, I thought, had they received bills after the style of my friend, Bill Bloggs.

"Dr. to Sir Probyng Lancet.
To: making 2 ft. incision in abdominal wall, removing 5 ft. of colon, joining lower end of small intestine to upper end of rectum and testing same for leaks, supplying, fixing and removing 24 mattress sutures .. .. 100 guineas.

The only drawback would have been that our waiting-rooms would no longer have re-echoed to the tales of our past triumphs. Instead our patients would have sat silently reading each other's bills.

* * *

As part of our Coronation celebrations members of the staff planted trees in the hospital grounds. It was a pretty expression of loyalty, but I cannot help feeling that in their unanimous choice of ornamental cherries they missed a big opportunity for self-expression. Would it not have been more appropriate, for instance,

if the psychiatrist had planted nuts? The geriatrician should obviously have provided an elder; the obstetricians a plot of gooseberry bushes; and the venereologist a hawthorn, because of its fruit and the number of pricks (intramuscular) which his calling demands. A bed of sweet peas outside the diabetic department might be rather old-fashioned, but what about a few sugar canes? The anæsthetists might well protest if offered a sycamore and ask for an olive, as they bring peace into the midst of turmoil. The surgeons could have any sort of tree that provides barber's poles, possibly an ash, though as stools are made from this the pædiatrician has prior claim. The orthopods could have roses on account of the fruit. Dermatology might be represented by an eczemous tree (useful on Dec. 25) well covered with lichen. The hæmatologist could look up from his rhesus grouping to see a monkey puzzle of another sort, and the pathologists would find something with a lot of dead wood outside the mortuary. Aspens might be shared by the neurologists, who deal with the shaking palsy, and the general physician and his thyrotoxic patients. Any G.P. who needed a quiet life could plant an apple, and night sister might provide a cocoa plant. The urologists should try ground-nuts, bladder-campion, or possibly some of the stone fruit. The administrative officer from headquarters could be invited down to put in a large box bush as rulers are made of its wood. Those who say that box is a euphemism for coffin would be asked to keep their mouths shut. We would welcome a contribution from the Editor of *The Lancet*, and he no doubt would choose a blue cedar, as we understand that that is what pencils are made from.

* * *

The frequent clotting of London traffic during these last few weeks has given rise in pathological circles to the fear that it may stop altogether through coronationary thrombosis.

* * *

A *perambulation* of pædiatricians seems an apt collective noun, though we were by no means pushed around when members of the local pædiatric club inspected a veterinary research unit last Saturday afternoon. Indeed, we were so interested that we abandoned the toddler's gait customary on these occasions, and fairly gambolled round the laboratories and grounds.

The magnificent bulls for artificial insemination attracted most attention. Lest we should imagine, however, that there are no problems in the bovine Welfare State, we were told of difficulties which do arise. For instance, spermatozoa whose ardour has been cooled during months of frustration in the ice-chest sometimes take it on themselves to go backward *au moment critique*.

Vets vie with even the most recently fledged pædiatricians in "cubicilisation," and they are far in advance of obstetricians in their devotion to the antenatal care of fathers, a prospect which produced envious comment from the males in our party—and some wholly male pædiatricians do, somewhat anachronistically, persist.

What would an older generation have thought of the fact that we saw not a single horse during our visit? We did, however, see three dogs, though they were visitors and not inmates. We were also informed that when Dartmoor ponies are turned loose in lush grass they tend to develop dermatitis, owing to the unaccustomed high level of chlorophyll in their diet. Clearly, we shall have to watch those children who use the modern, widely advertised toothpastes.

In the museum two exhibits astonished us. One was an example of osteopetrosis, which was casually attributed to virus infection; the other, a specimen of muscular dystrophy, which is regularly cured with methylene-blue. On Monday morning I expect to see a crowd of would-be therapeutists in the records department of the children's hospital, anxiously looking up names and addresses in the diagnostic index of patients.

* * *

He is wise who knows that he
Dust has been and dust must be.
But a fool is he who must
Fill the interim with dust.

Letters to the Editor

ONE-STAGE PROTHROMBIN-TIME TEST

SIR,—It is being gradually recognised that the simple one-stage prothrombin-time test was largely responsible for bringing blood-clotting out of the doldrums and confusion into which it had been plunged by reckless theories promulgated during the first third of the present century. So great was the bewilderment that the very existence of prothrombin was at times denied. It is beginning to appear as if the cycle of confusion is about to be repeated. The clear concept of prothrombin as a constituent of the blood which becomes diminished by depletion of vitamin K or after the administration of dicoumarol is gradually being dimmed by the introduction of a multitude of new factors such as proconvertin, factor VII, and co-thromboplastin. As a result of this trend, the one-stage prothrombin-time has again become the target for condemnation. To be sure, its clinical value and reliability is no longer denied or questioned, but now the accusation is that it does not measure prothrombin. The statement in your editorial of April 25 that "The use of the Quick one-stage clotting test (the doubts about the 'prothrombin' it measures have, we suppose, made 'prothrombin-time' out of order) . . ." epitomises the views that at present seem to be in the ascendancy.

Before dismissing summarily this test as a quantitative measure of prothrombin, it may be judicious to reconsider it in the light of some recent findings, particularly those on the prothrombin in the blood of the newborn infant. As is well known, when the prothrombin is determined by the two-stage method, it is found to be 30% or less, in spite of a normal prothrombin-time. It was in a vain attempt to explain the paradoxical results of the two-stage method that hypothetical prothrombin converting factors were first introduced. Yet one is still waiting for concrete proof that such agents exist as primary factors in circulating blood. Attempts to show their presence in blood in the newborn have failed.[1] The findings in infants' blood can be satisfactorily explained without introducing accelerator factors. The blood of both newborn and adults contains the same concentration of active prothrombin, which accounts for the normal prothrombin-time in both bloods.[2] In adults, however, the blood contains in addition a high concentration of prothrombinogen (inactive prothrombin), which is absent in newborn blood; consequently, the total prothrombin which is measured by the two-stage method is much lower in newborn than in adult blood. No agent such as factor VII need be postulated to explain the normal prothrombin-time of infant blood.

It seems reasonably certain that failure to recognise the existence of prothrombinogen in human blood has been largely responsible for the present array of hypothetical accelerator factors. In a recent publication [3] we have shown that the prothrombin-time remains a reliable measure of prothrombin, provided the procedure is carried out as originally outlined. The findings which are now attributed to converting factors can probably all be more simply re-interpreted by the conversion of prothrombinogen to active prothrombin.

If the reliability of the one-stage method is unjustifiably undermined, the interpretation of the prothrombin-consumption test would likewise become a hopeless jumble, despite the fact that this test furnished the first practical explanation for the coagulation defect of both hæmophilia and thrombocytopenia. It would be most unfortunate if progress in the thromboplastin-deficiency states were arrested by a deluge of new theories and

1. Quick, A. J., Hussey, C. V. *Proc. Soc. exp. Biol., N.Y.* 1953, **82**, 449.
2. Quick, A. J., Murat, L. G., Hussey, C. V., Burgess, C. F. *Surg. Gynec. Obstet.* 1952, **95**, 671.
3. Quick, A. J., Hussey, C. V. *New Engl. J. Med.* 1953, **248**, 624.

hypothetical factors that not infrequently owe their existence to laboratory tests which often seem to be more impressive in their name than in the validity of their control.

Milwaukee, Wisconsin. ARMAND J. QUICK.

TREATMENT OF HYPERTENSION

SIR,—Your annotation of April 25 reviewed with admirable brevity one side of this topic. It left other aspects barely mentioned. These can be approached through the viewpoint of 1933. We had then virtually no good hypotensive drugs. We assumed that in perhaps 95% of cases the hypertensive needed his high arterial tension to provide adequate circulation to his vital organs (to what extent we were emulating the fox contemplating the desirables beyond his reach I cannot say). The past twenty years are noteworthy for the accumulation of data which warrant the abandonment of that concept; but many practitioners, in my country at least, are not aware of this.

Perhaps the early work with thiocyanates was responsible for the beginning of the collapse of the concept. In those few cases where irregularities of excretion, skin rashes, &c., were long enough delayed (by blood-level control or by good luck) real reductions in blood-pressure were shown to be well tolerated.[1] Soon the results of sympathectomy in favourable cases showed that many patients could function normally at much reduced arterial pressures. The revival of *Veratrum viride* which followed the preparation of dependable, purified, and standardised extracts contributed similarly, since it quickly became clear that parenteral administration would strikingly lower the blood-pressure of virtually 100% of hypertensive patients.[2–6] At the resulting lower levels of blood-pressure, which were often within the normotensive range, these patients could walk about and experienced no postural hypotension, and no embarrassment of cerebral, renal, or hepatic function. The presence of a slow heart-rate emphasised that normal function in the hypertensive at lower pressure was not gained at the expense of increased cardiac activity. Despite their unphysiologic mechanism, hexamethonium salts have likewise contributed evidence of the capacity of the hypertensive to get along with reduced pressure.

A direct result of this alteration of concept has been the enhancement of value attached to agents reducing pressure in individual cases. Much improvement can be gained for certain patients from particular drugs.[6 7] It becomes important now to stop rejecting drugs which on oral administration effectively lower hypertensive blood-pressures in only a limited percentage of cases. We need to screen the active hypotensive agents in each patient in an orderly way, to find out which drug acts best for him. We need to weigh the improvement the patient obtains from therapy against the dangers of toxic actions and against the discomforts of side-actions produced by each drug. Recently it has become clear that combinations of these drugs increase the percentage of patients who will respond and make possible reduction in discomfort due to side-actions.[8 9]

The past ten years have focused attention on four agents worth screening in this orderly manner. Of these, three are drugs of great potency. The fourth, *Rauwolfia serpentina*, is a basal agent.[10 11] Rauwolfia's mild action, its vagotonic effects, its freedom from side-actions, its ease of management consequent on low increment of response with dose (increasing dosage beyond the minimal effective produces neither excessive fall in blood-pressure nor severe side-effects), and its very low toxicity combine to make it a basal hypotensive analogous to the ideal basal anæsthetic (nitrous oxide?). Rauwolfia, like veratrum, requires careful identification, extraction, and standardisation if its advantages are to be obtained fully. 'Rauwiloid' is a proprietary compound that may fulfil these criteria.

The three full-potency hypotensives, while imperfect, are far ahead of classical substances. Your annotation made no mention of standardised *Veratrum viride* extract ('Veriloid' is an example). Oral administration of this agent deserves mention because it is the safest of the three (no risk of organ toxicity, widest margin against lethality), and because it will produce excellent results in 20–40% of patients.[12] Its outstanding disadvantage is the narrowness of the range between good hypotensive effect and emetic side-action, which makes management difficult. The spread between hypotensive and emetic doses appears to be widened by combination with rauwolfia.[8] Thus the percentage of patients controlled by veratrum may be much improved.

From hexamethonium salts one can obtain the greatest hypotensive action. Acknowledging the side-actions and dangers mentioned in your annotation, recent work has revived hope that these compounds can be useful by mouth, since rauwolfia apparently can reduce the required dosage and the incidence of side-actions.[9]

Hydralazine is a useful agent despite tolerance and the unpleasant side-actions of headache and tachycardia; but the risk of toxic effects (drug rash, drug fever, possibly agranulocytosis [13]) must be weighed. Combination with rauwolfia and even with hexamethonium seems, from recent reports, to offer much advantage.

In summary, I do not agree that the immediate prospects for helping the individual hypertensive are still poor. If we use the tools now available against the disease, our patients will benefit in proportion to our skill.

Los Angeles, California, U.S.A. GEORGE L. MAISON.

POLIOMYELITIS

SIR,—The case described by Mr. Hyman (April 25) exemplifies the danger of over-exertion during recovery from poliomyelitis. I do not agree with Dr. Ritchie Russell (May 2) when he brushes aside too-vigorous exercise as the cause of the deterioration of muscle-power in this case.

Between the antiquated method of rigid splinting and exercises to the point of fatigue there is such a range of possible variations that it is difficult for the less experienced to decide which to adopt. In the subacute phase it is difficult to estimate from the, sometimes scanty, symptoms the stage of the lesion.

With regard to the handling of affected limbs, I try to avoid the muscles of, for example, a painful calf being pressed by the "dead weight" of the tibia. In a few cases of very painful calves I have used what might be termed an "air-cushion gutter-splint," consisting of two inflated lengths of bicycle inner-tubes. These tubes are glued with latex to a length of 'Sorbo' in such a way as to form a gutter with varying width according to the shape of the calf. Thus the lower leg is gently supported at both sides of the midline from the heel to the back of the knee, the midline itself remaining free from any pressure. A layer of gauze cotton-wool is placed on the rubber to prevent condensation. Any device can be added as a foot support. I have found very tender lower limbs surprisingly comfortable with such an arrangement.

1. Barker, M. H. *J. Amer. med. Ass.* 1936, **106**, 762.
2. Meilman, E., Krayer, O. *J. clin. Invest.* 1949, **28**, 798.
3. Stearns, N. S., Ellis, L. B. *New Engl. J. Med.* 1952, **246**, 397.
4. Goldman, R. W., Frierson, H. R. *Amer. J. Med.* 1953, **14**, 168.
5. Kauntze, R., Trounce, J. *Lancet*, 1951, i, 549.
6. Wilkins, R. W., Stanton, J. R., Freis, E. D. *Proc. Soc. exp. Biol., N.Y.* 1949, **72**, 302.
7. Mills, L. C., Moyer, J. H. *Arch. intern. Med.* 1952, **90**, 587.
8. Wilkins, R. W., Judson, W. E. *New Engl. J. Med.* 1953, **248**, 48.
9. Ford, R. V., Moyer, J. H. Unpublished data.
10. Vakil, R. J. *Brit. Heart J.* 1949, **11**, 350.
11. Ford, R. V., Livesay, W. R., Miller, S. I., Moyer, J. H. *Med. Rec. Ann.* (in the press).
12. Kauntze, R., Trounce, J. *Lancet*, 1951, ii, 1002.
13. Kaufman, M. *J. Amer. med. Ass.* 1953, **151**, 1488.

May I add one word about the transfer of poliomyelitis patients from fever hospitals to other units for further treatment. Transfer after 3 weeks, as now practised, should be regarded as an expedient to ease the burden of the fever wards—not as justified from every point of view. Opinion on the danger of spread of infection after this period is not yet unanimous; and, even after these first 3 weeks, treatment is still—except in very mild cases—restricted by pain and the general after-effects of the illness. The later the patient is exposed to exercises to the point of fatigue, the better.

Wakefield. OSKAR TURGEL.

ANTICOAGULANT DRUGS

SIR,—Mr. Rowden Foote (May 16) is concerned about conflicting opinions regarding deep-vein thrombophlebitis.

In the United States the split is between advocates of anticoagulant therapy and advocates of ligating and/or resecting veins—even including the inferior vena cava!

As to dicoumarol causing the skin eruptions—or for that matter any toxic manifestations except hæmorrhage—absolutely No, Professor Boyd and Mr. Foote. No, never!—with hardly a *Pinafore* qualification.

We make a distinction between "thrombophlebitis" (i.e., milk leg) and "phlebothrombosis." The former is self-explanatory, implying an inflamed vein with clotting of blood within the vein. This condition rarely causes embolism. Apparently this is what Professor Boyd refers to as "deep-vein thrombophlebitis."

Phlebothrombosis refers to the almost silently developing intravascular clotting developing, for example, in calf and foot deep veins. Pulmonary embolism is fairly common in this type—in fact it often occurs before evidence of "phlebothrombosis" is noted. We in the New York area (and I think through most of the country outside of Boston) rely almost entirely on anticoagulants in these cases—beginning with heparin plus dicoumarol, and dropping the heparin in two days or so when daily prothrombin tests have shown that dicoumarol is becoming effective.

Scarsdale, N.Y., U.S.A. BERTON LATTIN.

THE NURSE'S RESPONSIBILITY

SIR,—Your leading article of June 6 and the subsequent letters from Dr. R. E. Smith (June 13) and two members of the nursing profession (June 20) cover very rough ground and anyone who joins in the discussion may well stumble!

Surely this new problem of how much a nurse should be expected to do in the management of the sick patient is yet another expression of the increasing fear of litigation which is dominating hospital policy and regulation. Professional bodies in medicine and nursing, no less than the many hospital authorities, are seeking to protect themselves from persecution by their patients. The welter of circular letters issued by regional boards and by the Ministry itself is an endeavour to manage the whole of medicine by regulation. If the nursing staff—that is the trained staff—are to be restricted to what some would call the "maternal" aspects of nursing, who then is prepared to undertake the scientific work involved in modern treatment?

There is a gross shortage of house-officers; consultant clinics are overloaded; waiting-lists are large, and in many hospitals lack of operating-theatre accommodation restricts the turnover. Medical treatment is team-work, and any member of the team, no matter what his or her official training has been, must surely be prepared to undertake such tasks as are delegated by the leaders of the team. We are repeatedly hearing warnings that the nurse must not be turned into a "non-registered doctor," but modern surgery in particular demands that skilled nursing must be based on scientific understanding. Much of the nurse's interest in her work in the past has been lost by "parrot-wise" teaching in which the nurse has learnt the answers to questions she may be asked in examinations, but has had no real understanding of the meaning and purpose of her actions.

Those who accept any part in the treatment of the sick must also accept responsibility which cannot be defined by rules and regulations. Herein lies the difference between the clinical staffs of our hospitals and the lay administration, which, though it may fail to provide the personnel and facilities for adequate treatment, is always itself protected by the fact that it (the impersonal administration) has had no contact with, or personal responsibility for, the patient. If the restrictive ideals which have now been suggested were put into practice, many of our hospital beds would be put out of action. We are much dependent upon the work which our nurses undertake beyond their training syllabus, and indeed beyond the number of hours officially allotted for their duties. Any suggestion of "working to rule" must never be allowed to come into our hospital service on the professional side, no matter how much we are all provoked by the many impositions placed on both medical and nursing staffs as the public and its legislators continue in their struggle to squeeze a quart into a pint pot.

London, S.E.19. D. F. ELLISON NASH.

IMMEDIATE RESULTS OF SANATORIUM TREATMENT

SIR,—In 1951[1] I described the results of treatment, judged by "sputum conversion," of male adult patients discharged from Colindale Hospital in the years 1938–50. These totalled 3332; but after deducting sputum-negative patients, and those whose stay was too short for conversion to be attained for three consecutive months before discharge, 2472 entered the survey.

Up to 1947 the conversion-rate was below 29%, but it rose in 1948 to 36%, in 1949 to 55%, and in 1950 to 63%. I attributed this improvement partly to the admission of less advanced cases, but mainly to the effect of streptomycin and *p*-aminosalicylic acid.

I can now bring the investigation up to date, by giving results for 1951 and 1952, during which 731 male patients have been investigated; of these 385 were sputum-positive and stayed long enough to satisfy the criteria for sputum-conversion. The following is a summary of the results:

Year	Sputum-negative	Sputum-positive on admission		Converted	Total	% conversion
		Not converted	2/12-converted			
1951	170	64	10	111	185	60
1952	176	70	10	120	200	60

The conversion-rates of 60% attained for both years are slightly lower than for 1950 (63%); and, although I previously expressed the view that, as chemotherapy was now fully exploited, the curve was likely to flatten out, this actual fall, though slight, deserves some explanation especially in view of the introduction of isoniazid in 1952.

The above summary shows that in 1951 and 1952 no fewer than 346 patients (47%) were sputum-negative. In 1950 the corresponding proportion was 37% and in previous years it was 22% or less. Of the 176 sputum-negative cases in 1951, 121 (68%) had been sputum-positive at some previous date, commonly shortly before admission, and of 100 consecutive admissions

1. Snell, W. E. *Lancet*, 1951, ii, 415.

taken at random at least 60 had received "chemotherapy" either at home or in other hospitals before admission. In other words, those cases which were amenable to conversion by bed rest and chemotherapy had been converted before admission, leaving a more resistant group to enter this survey.

A factor hindering improvement in conversion-rates is the number of middle-aged (over 45) patients who, because of delayed diagnosis with resulting irreversible changes in the lungs and chronic respiratory disability characteristic to their years, and consequent unsuitability for surgery, often constitute insoluble problems in treatment. My 1951 paper showed that the chances of conversion regularly receded with advancing years, and the new figures, though small, support the previous findings:

CONVERSION BY AGE-GROUPS. 1951 AND 1952

Age (years)	Not converted	2/12 converted	Converted	Total	% conversion
Under 20 ..	5	1	11	17	..
20–29 ..	30	6	94	130	72
30–39 ..	37	5	67	109	61
40–44 ..	16	2	22	40	55
45 and over	46	6	37	89	42
Totals ..	134	20	231	385	60

In view of changing fashions in treatment, it may be again of interest to note the methods by which conversion was attained; but the increasing complexity of treatment makes classification ever more difficult. The accompanying table indicates the broad lines by which success was achieved. Comparing the two years, the second shows fewer conversions by artificial pneumothorax and thoracoplasty, a static number by plombage, and more conversions by resection and especially (perhaps surprisingly), by pneumoperitoneum, which was of course associated in most cases with chemotherapy. Over the previous twelve years the main treatments producing conversion were artificial pneumothorax 35%, routine treatment 21%, and thoracoplasty 17%. Owing to the widespread use of chemotherapy and the greater variety of surgical treatment, conversions by routine treatment alone are now very few; but the sanatorium régime nevertheless remains, for all patients, the fundamental basis of treatment.

Summary.—In this investigation sputum conversion is held to have taken place when the sputum has been found free from tubercle bacilli on direct examination and culture, for the three consecutive months preceding discharge. (Patients converted for the final two months only are also recorded but are considered as unconverted.) Of 385 sputum-positive patients treated at Colindale in 1951 and 1952 231 (60%) underwent conversion. Of the 346 sputum-negative patients admitted during this period, approximately 68% had been sputum-positive shortly before admission: they had undergone conversion mainly by "chemotherapy," leaving a relatively resistant group who were still sputum-positive when admitted. Of the sputum-positive patients 23% were aged 45 or over—the group least susceptible to conversion. Comparing the last two years at Colindale more conversions have been obtained by resection or pneumoperitoneum, and fewer by artificial pneumothorax or thoracoplasty.

Colindale Hospital,
London, N.W.9. W. E. SNELL.

MEDICAL HISTORY OF THE SECOND WORLD WAR

SIR,—In your review (June 13) of the *Medical History of the Second World War* you remark that the book is unlikely to raise the pulse-rate of many of those who served under the motto *Per arduis fidelis*.

I think it possible that the blood-pressure of many of those who served in the R.A.M.C. (at any rate of those who have had the advantage of a classical education) may be raised, when they see their noble motto so vilely misquoted.

Wakefield. G. E. MACALEVEY.

*** We apologise for our inadvertence. The motto is, of course, *In arduis fidelis*.—ED. L.

OBSERVATIONS ON PEPTIC ULCER

SIR,—It is not for me to discuss the physiological aspects of Dr. Csato's original and stimulating letter (May 16). But may I draw attention to the crucial change of attitude towards a certain interesting group of diseases implied in his approach?

The emphasis he places on periodicity as opposed to the static evidence of the X-ray plate has a relevance far wider than merely to the treatment of peptic ulcer. It adds, in fact, the fourth dimensional quality of time/motion to the consideration of those diseases in which periodicity plays a major part. As he rightly claims, periodicity is a factor which has often been noted, but in treatment consistently ignored.

Among philosophers Heraclitus, echoed centuries later by Bergson, has compelled recognition of time and motion as prime factors in the structure of the Universe; and it is now some time since physicists discovered, to their temporary confusion, that the weights of certain things were different when in motion than when at rest. But medicine, as far as treatment is concerned, doggedly persists in its static, three-dimensional approach

TREATMENT USED IN CASES SHOWING CONVERSION

Treatment	1951	1952	1951 and 1952
Artificial pneumothorax (right)	8 } 28 (2 had P.P.)	8 } 17	45
" " (left)	11 }	5 }	
" " (bilateral) ..	9 }	4 }	
Thoracoplasty (right)	25 36 (4 had contralateral A.P.;	13 28 (2 had contralateral A.P.; 1 had	64
" (left)	11 1 had P.P.)	15 contralateral plombage)	
Resection (partial)	8 } 10	11 18 (2 had contralateral A.P.; 1 had	28
Pneumonectomy	2 }	7 phrenic crush)	
Plombage (right)	7 } 14 (2 had contralateral A.P.;	6 15 (1 had contralateral thoracoplasty;	29
" (left)	6 } 1 had phrenic crush)	7 2 had contralateral A.P.; 1 had	
" (bilateral)	1 }	2 P.P.)	
Extrapleural A.P.	1 1	0	1
Pneumoperitoneum	12 12 (4 had phrenic crush)	29 29 (1 had phrenic crush)	41
Chemotherapy alone	9 9	11 11	20
Routine	1 1	2 2	3
Total	111*	120†	231

* 73 had "chemotherapy" in addition. † 99 had chemotherapy, including 20 treated with isoniazid.
A.P. = artificial pneumothorax. P.P. = pneumoperitoneum.

to that most temporal and motionable of entities—the human organism. The real originality of Dr. Csato's contribution will not, I hope, be sidetracked as just one more therapeutic suggestion for a single ailment.

London, W.1. ALAN MCGLASHAN.

HOSPITAL COSTING

SIR,—The letter from "Administrator" (June 20) calls for a response from me. I read with interest that he assumes that I am "unaware not only of the lessons of practical accounting but also of the important psychological advantages that can flow from purposeful accounting in terms of individual responsibility."

I had some ten years' experience of practical accounting, both in the profession of accountancy and in industry. During this period I became a chartered accountant, and subsequently engaged in reorganisational work in large-scale industry—particularly in connection with clerical routines. All this was years ago, but the essential problems are still much the same; punched-card routines, the problems of the unreliability of primary data in costing schemes (time-sheets, &c.), the difficulties of seeing the wood for the trees—these are still features of the accounting landscape.

"Administrator" appears to be defending the principles of cost-accounting against the ill-informed doctor; I sympathise with his imagined predicament, but I am sorry that he should thus misunderstand my article (May 16), for I am primarily interested in achieving real coöperation between doctors and administrators. His anxiety to defend himself against imaginary attack leads him to make criticisms which are I think unjust. I devoted some space to emphasising the need for extracting items of expense which were controllable by the individuals concerned, so that individual responsibility should be fostered; yet "Administrator" accuses me of being unaware of this necessity!

He considers that my object of "providing a corrective to any too-enthusiastic adoption of detailed schemes" is at variance with the title of my article; I cannot see this. This criticism would be valid only if my object had been the exclusion of anything to do with costing from hospital accounting.

The terms "subjective" and "objective" in costing parlance are quite clear in their meaning to accountants and administrators—but my article was addressed primarily to doctors, and they might be forgiven if they expected these words to have the meanings assigned to them in ordinary speech. Hence my brief explanation that, in costing practice, each operated as an extension of the other. My simple little diagram to illustrate this process was introduced solely for this purpose; your correspondent's attempt to read into this diagram a detailed scheme, as if a costing system were a huge grid of rows and columns in a literal sense, is surely unjustified; I cannot believe that he really thought I meant just that.

It is true that "to accent the objective classification of expenditure does amount to a fresh outlook"—but the *freshness* of this change is felt mainly by those trained in the subjectively orientated accounting systems. The idea was fresh to me, twenty years ago—but lay people do not suffer from the disadvantages of such a training, so there was no need for me to labour the point in an article addressed to doctors.

Your correspondent's grumble that (in my suggestion that statistical statements should be adapted to the various tiers of administration) I omitted to mention the individual hospital, is unfounded: I referred to the obvious fact that hospital management committees review the costs of running "the various separate clinics and hospitals within their group."

Possibly my warning against the misuse of costing systems was "platitudinous"—but maybe I shall be forgiven, for it was also "no doubt much needed." Just how much this warning may be needed in the future is problematical, but I may refer "Administrator" to one of the three reports on hospital costing now available, in which he will find that the detailed time-study of surgical operations is envisaged as part of an interesting research project. Is it impossible that this might lead some readers to suggest that, for example, a subtotal thyroidectomy should take x minutes? Can your correspondent not see that some enthusiastic technicians in time-and-motion study might write down as "unproductive time" that interval in which the surgeon is not visibly acting, but thinking?

It is precisely *because* I have seen the enthusiast in action that I warn my colleagues against this kind of "too-enthusiastic adoption of detailed schemes."

I assure "Administrator" that I normally use the right end of my microscope; but, if some costing enthusiasts had their way, I might find myself having to take a bus journey to another laboratory to visit the microscope installation, there centralised so that a shift system could be operated—"thus raising to a more satisfactory level the percentage usage of the instruments" (I quote from a possible future Costing Report to the Minister).

To be serious, I repeat my plea that doctors and administrators should discuss the whole problem. No-one likes being administered, and no-one likes being ill; but administrators and doctors are often quite pleasant people. Both have problems—and opportunities—of avoiding the most irritating features of costing systems in the context of hospital work.

Let it be recognised that there is a likelihood that doctors may be a little on the defensive (or just not interested) in relation to costing schemes; and that administrators also may be a little sensitive when alterations in accounting procedures are contemplated. If this is the situation, then surely informed discussion will clear the air?

London, N.W.3. A. F. MOHUN.

SIR,—Mr. R. S. Murley (June 6) takes me to task for suggesting that low bed-occupancy rates imply inadequate use of hospital beds. I can best reply by quoting the experience of our hospital in recent years. Pressure on our beds had greatly increased, as the number of new outpatients referred to us had gone up by 20% a year. Nevertheless, without an increase in beds, we have done much towards dealing with the resulting increased demand for admissions. This has been done by raising the bed-occupancy rate and by reducing the average length of stay, *without any apparent loss of medical efficiency*. The following figures are quoted from the last available annual report (1951):

—	1949	1950	1951
Beds			
Complement at end of year ..	853	862	862
Daily average number of beds occupied	769	806	807
Percentage of available beds occupied	90·15	93·5	93·6
Discharges and deaths during the year	13,684	14,431	15,639
Average length of stay (excluding confinements, pulmonary tuberculosis, mental observation, and chronic sick) in days	18	17·05	15·85
Outpatients			
New patients (excluding casualty)	24,355	30,254	34,089

The changes in the indices may not appear impressive until it is appreciated that, with virtually the same number of beds, we have admitted a further 2000 patients a year—an increase of 15%, and equivalent to building a 100-bed extension. This achievement has been made possible by having a whole-time admission officer and a geriatric physician, by the careful planning of elective

admissions by all members of the senior staff, by the excellent coöperation of the pathological and X-ray departments in the rapid introduction of new methods of diagnosis and in the control of treatment, and because the level of medical and nursing staffing was adequate.

The bed-occupancy rates reported in the Ministry's Annual Costing Returns, to which I referred in my previous letter, reveal extraordinary discrepancies between hospitals of a similar type doing the same class of work. Even more striking are the variations in the average length of stay (as yet unpublished). Taking five large general hospitals, in Greater London, chosen only for their similarity of function, the average length of stay per patient is recorded as 27, 25, 19, 19, 16 days, with bed-occupancy rates of 77·0, 89·6, 90·8, 82·0, 83·2 respectively.

I am fully prepared to admit that there may be important fallacies in relation to many of these mass hospital statistics. There may be a difference between the working total number of beds and the figures recorded by the hospital administrators; beds long since taken down may still appear in the administrative total from which the bed-occupancy rate may be calculated. The association of chronic or convalescent units must be taken into account. The lowest average length of stay for a large general hospital in this country is only 12 days, but this particular hospital has a big convalescent unit closely associated with it. It is important to distinguish between optimum and bare minimum length of stay; a shorter length of stay for a particular disease does not necessarily imply better treatment. While appreciating these fallacies, from my own personal observations I suspect that the wide variations in these indices mainly correlate with the numerical adequacy of the medical and nursing staff, and if this is so, it is important that it should be clearly and officially recognised.

My point, which I maintain is a reasonable one, is that in spite of possible fallacies, the wide variations in these indices, together with our own experience, suggest that some hospitals are using their available beds inadequately and that this is an extravagance which the nation cannot afford. Hospitals are a particularly expensive social service, and it is reasonable that every effort should be made to ensure that the maximum use is made of their facilities—particularly of beds related to the expensive ancillary departments.

Lay members of medical committees are perfectly right in raising queries about bed-occupancy and similar indices of hospital efficiency and in seeking assurance that the problem is being studied. However, they should realise that the subject is a complex one which can be dealt with adequately only by senior medical and nursing staff and the administrators—who must be prepared to recognise the existence of a problem and study its solution. Once any problem is defined, one is already half-way towards a solution. Simple measures may help enormously. In one large Midland hospital it was customary to discharge patients in the afternoon, and by a local nursing tradition the beds were not filled until the following day. By discharging patients in the morning and filling the beds the same day (except those for duty admissions), the hospital made some 6000 extra bed-days available each year—sufficient for the admission of another 300 patients.

Mr. Murley is quite wrong, I believe, in suggesting that an increased turnover almost inevitably means a fall in the percentage bed-occupancy. Indeed the reverse is the truth.

I wish to underline my previous statement that a general community hospital should have at least a 90% bed-occupancy and that 93% is perfectly feasible. My private opinion is that even this figure could be increased by further reorganisation; and indeed last month we recorded a 96% bed-occupancy. The wider application of our experience should result in an appreciable fall in waiting-lists. Mr. Murley says that "unoccupied hospital beds are surely less of an extravagance than an unnecessarily occupied one." My point is that if there are these unoccupied beds, as suggested by the Hospital Returns and confirmed by Mr. Murley himself, they should be mobilised to deal with the national waiting-list, which stands at approximately 500,000. There is a strong case for every hospital medical advisory committee to review carefully its own experience. I anticipate that the King's Fund report will make many practical suggestions which could be implemented.

Central Middlesex Hospital,
Park Royal,
London, N.W.10. F. AVERY JONES.

INJURIES OF SPINAL CORD

SIR,—In your annotation last week you refer to experimental injuries produced in rats and dogs. Then you go on to state that "the direct trauma used in these animal experiments is not really comparable with the indirect trauma which commonly causes spinal injuries in man." Of course it is not, nor is it likely that early incision of the pia and posterior myelectomy in cases of human spinal injuries will produce good results. I maintain that such experiments, apart from causing needless suffering especially to dogs, is a sheer waste of time. My confirmed belief is that on the whole animal experimentation has become an obsession and is not furthering our knowledge of practical medicine or surgery.

Edinburgh. JAMES BURNET.

PREVENTION OF POSTOPERATIVE CHEST COMPLICATIONS

SIR,—We would like to draw attention to a misquotation in Dr. Davidson's article last week.

According to this article, a description of the use of benzocaine and urethane for the treatment of painful stumps was given by Ritchie Russell and Spalding in 1950. There is, however, no reference to benzocaine urethane in the article referred to,[1] which deals with percussion therapy for painful stumps. The description of the use, and the principle underlying the mode of action, of benzocaine urethane was published by Kohn and Vitali in August, 1950,[2] following the article of Ritchie Russell and Spalding.

As to the rationale of Dr. Davidson's method, it is not clear why benzocaine should be first made up in oil and injected separately before the urethane is introduced. Injected oil is not always well tolerated; and there does not seem to be a necessity for introducing it, since benzocaine in a proportion of 2% is well soluble in an aqueous urethane solution and it can therefore be injected as such a solution. The effect is the same—i.e., the formation of microcrystalline deposits of benzocaine in the tissues. Benzocaine, being insoluble in water, is almost immediately precipitated by the watery tissue fluids, and the urethane is absorbed.

In connection with the increasing interest in the problem of local anæsthetics of long action it might be worth mentioning a few data. Benzocaine in urethane was first introduced, and its mode of action described, by Rappaport[3] in 1946, and its clinical application reported by Spiro.[4] Following their publication a 2% solution of benzocaine in urethane was manufactured by Messrs. Zori, of Tel Aviv, under the trade name of 'Prolongal-Benzocaine.' Further reports were published by Dresel,[5] Rachet et al.,[6] Hirsch in Scandinavia, and others.

1. *Brit. med. J.* 1950, ii, 68.
2. *Ibid*, p. 415.
3. *Acta med. orient.* 1946, **5**, 115.
4. *Ibid*, p. 119.
5. *Ibid*, 1949, **8**, 43.
6. *Arch. Mal. Appar. dig.* 1950, **39**, 242.

In this hospital a benzocaine urethane solution, prepared in our own dispensary, has been used for a variety of orthopædic and surgical conditions since 1949.[2]

The application of benzocaine urethane in upper abdominal surgery was reported by Winkler in 1951,[7] and in this country by Rutter in 1952.[8] It might also be interesting to note that first reports on another local anæsthetic of long action—namely, 'Efocaine'—were not published in the U.S.A. until 1952 (without, by the way, any references to the previous work on benzocaine urethane, the use and mode of action of which are based on exactly the same principle as efocaine).

Queen Mary's Hospital, Roehampton.

J. KOHN
M. VITALI.

JUNIOR HOSPITAL STAFFING

SIR,—The article by Dr. Forrester in your issue of June 13 is very interesting and stimulating; but it is, I think, misleading in its comparison of the incomes obtainable by the whole-time specialist and the general practitioner. Out of his £3000 the latter has to find a considerable sum for expenses, while the former does not need to supply even a stethoscope or a sheet of notepaper.

The glittering prizes of the specialist are admittedly now very rare, but on the other hand the early years are surely much better than in the old days even allowing for the changed value of money. But was it the financial side of the glittering prize which induced a young man to take up a specialist career?

Wirral. K. COBBAN.

LOCALISED MUSCULAR ATROPHY IN DIABETES

SIR,—I was interested in the comments of Dr. Harris-Jones (May 30) and Dr. Robertson (June 13) on the tentative view expressed in my note on isolated muscular atrophy in diabetes. On photographic rather than bedside evidence we are unlikely to agree as to whether a muscular component was or was not present in the lesions described. It is noteworthy that relatively non-fatty regions—the jaw and thumb—were involved in one case. In the absence of surgical exploration (a hole cannot be subjected to biopsy) doubt must exist.

However, the existence of "space-vacating" lesions in diabetes unrelated, at least in site, to insulin injections is not in doubt, although apparently it is not commonly recognised. To accept such lesions, again in the absence of histological investigation, as ectopic insulin atrophy is not entirely helpful. An explanation becomes necessary for an insulin effect which is simultaneously both localised and yet quite remote from the site of injection.

Royal Northern Hospital, London, N.7. CEDRIC HIRSON.

TROUBLESOME TAPEWORMS

SIR,—The course of treatment for tapeworm recommended by Dr. Asher (May 23) lasts 4–5 days and has to be carried out in hospital. Whilst serving with the R.A.M.C. at the 43rd General Hospital, I introduced the following simple treatment:

The patient is admitted to hospital at lunch-time and is given a light meal. At 3 P.M. 2 teaspoons of magnesium sulphate are given as a purge. At 7 P.M. the patient gets for supper chopped herring with onions, 1 piece of toast, and a cup of tea without milk. At 6 A.M. next morning the patient is given 0·25 mg. of atropine, and at 7 A.M. a duodenal tube is introduced into the stomach. Every 10 minutes the tube should be advanced about 2 cm. until by aspiration with a syringe it is confirmed that it has passed into the duodenum. Now, 8–10 ml. of extract. filicis in 20 ml. liquid paraffin as an emulsion is passed through the tube into the duodenum. Usually at about 10 A.M. the complete worm is passed. If it is not passed by then a dose of magnesium sulphate should be given, followed 2–3 hours later by a high enema with fol. sennæ.

This treatment is completed in less than 24 hours and can be carried out in hospital or at home. I do not remember the number of cases we treated in this way, but it was quite considerable. There was never a failure.

Petah-Tiqvah, Israel. E. FRANKL.

BREAD

SIR,—May I congratulate you on your leader last week, as well as on your able review of the controversy over flour improvers (March 21)?

Bread is the staple food of the population of Great Britain, and no economic change is likely to alter that. The quality of the national diet, based on this staple, itself contributes largely to the health, or morbidity, of our population. Experience shows that a diet based on whole wheat flour has kept other peoples relatively free from disease, and experiment has shown that diets of the same specification have also kept rats in health (R. McCarrison). Again, at the Rowett Institute near Aberdeen it has been demonstrated that not only deficiencies in the B group of vitamins but also inbalance of that group affects growth. The case for first-quality bread rests therefore not only on intuitive understanding but also on such experimental biological evidence as is available.

In his Sanderson-Wells lecture the arguments which Professor Dodds brings to the "brown versus white bread controversy" rest not on biological or medical experiment but on history, economics, and politics. What you call "economic and commercial convenience" stems no doubt from the vast capital investments in the milling and baking trades. It is in the interest of these investments that the present customs of their trades be maintained. Enlightened professional and public opinion is uneasy that the bread policy of the nation should be so largely governed by the investment policy of the past. Does this policy contribute to the high national morbidity? Let us say that we do not know, and then the best opinion will demand that we use every resource to find out.

It was disturbing to find Professor Dodds, with the secretary of the Medical Research Council in the chair, asking "who is going to do this work?" and opining that "the charge, surely, should not fall on public funds." If a question which touches the health of the whole population should not be a charge on public funds, and if other research endowment cannot finance such inquiries, the public must question the whole structure and administration of the moneys on which research depends. If those who have a virtual monopoly of the means cannot "do the work," then reform—which many of us believe is overdue—is surely called for.

With great respect, it seems to me a pity that Professor Dodds's review of the problem of chemicals and food should contain so little evidence of a scientific kind.

East Suffolk and Ipswich Hospital, Ipswich. K. E. BARLOW.

SIR,—May I congratulate you on your fiery and courageous leader last week, taking up the cudgels laid down by your illustrious predecessor Thomas Wakley a hundred years ago. It ought to be brought home to the public that the addition of the arbitrarily chosen "token" nutrients (aneurine, nicotinic acid, and iron) to white flour still leaves it with a lower (probably much lower) nutritional value than the 80%-extraction National flour.

While I agree with Professor Dodds about the importance of modern food technology, as a doctor I find it disturbing to see the chemical manipulation of food considered on the same level as technical advances in heating, housing, or transport. Have we to put up with agene and other "improvers" on a national scale only because the small baker in this country has been replaced by big-scale "plant bakeries"?

7. *Wien. med. Wschr.* 1951, **101**, 692.
8. *Brit. med. J.* 1952, **ii**, 1418.

It has occasionally been argued that the digestibility of bread prepared from high-extraction flour is inferior to that of white bread. I may have been particularly fortunate with my dyspeptic patients, but I hardly remember anyone suffering from peptic ulcer who could not enjoy whole-meal bread after proper instruction how to take it.

London, W.1. Z. A. LEITNER.

RELIEF OF MENTAL HOSPITALS

SIR,—May I suggest that, to relieve our overcrowded mental hospitals, every suitable general hospital should set aside two small wards each of, say, 10 beds for male and female patients with affective disorders whose condition does not necessitate treatment in a mental hospital. Patients with nervous disorders have as much right to be treated in general hospitals as maternity, surgical, or medical cases. A trained registrar could be put in charge of these psychiatric units and the work supervised by a visiting consultant. Minor psychotherapy could be carried out there, and refractory cases could be referred to a mental hospital.

The advantages of such a measure would not be limited to the relief of overcrowding. Patients with affective disorders are likelier to respond to treatment in a general hospital than in a mental hospital, where for the time being neurotic patients have to be mixed with chronic incurable cases. Moreover neurotic patients would escape possible stigma in the public's view for having been treated as "mental patients." Lastly, the general hospitals themselves would benefit; for house-officers would be able to familiarise themselves with the management of mental patients. The arrangement would bridge the artificial gap dividing those who treat physical disorders from those who treat mental disorders.

Powick Hospital, Worcester. J. W. MULLNER.

THE ILLEGIBLE CANDIDATE

SIR,—Everyone will agree with Mr. E. W. Playfair (June 13) that bad handwriting is to be condemned. Everyone will also congratulate him on having learnt, at the age of 22, to write well after a few hours' lessons, spread over a few days, and will also admire his signature. My experience is, unfortunately, very different. When I was 21, I was told by Dr. Walter Morley Fletcher that, although he could read my writing, I must try to improve it. I spent the Christmas vacation going to Clark's College, Chancery Lane, three or four days each week, and was taught to write in the way the girls who were sitting for the Post Office examination wrote. I also practised hard for the next two years, and the legibility of my handwriting was greatly improved; but it was very difficult to maintain it in the stress of examinations and in writing notes at hospital on my knee. Now that I am old, I have writer's cramp if I do much writing. I can still write legibly if it is necessary, but it is a slow and painful process. My usual writing is bad.

The ability to write well varies as much as the ability to play games. Everyone seems to expect a boy or girl to be able to write well without any difficulty, though no-one expects people to be equally good at games. For instance, some people, having great ability, learn to play golf very easily, and soon reach a "handicap" of scratch; some after a few lessons likewise improve easily and reach a low "handicap"; others, like myself, after many lessons and much hard practice attain a moderate "handicap." Others, no matter how many lessons they have, or how much they practise, never attain a "handicap," and give up golf in disgust, and find some other means of taking exercise or spending their time. Unfortunately, people who cannot improve their handwriting still have to go on writing, and so distress the recipients of their letters, especially when they do not type their names under their signatures. It is possible that if I had been taught by another method I might have written better; but I am afraid I should never have been a good writer. Similarly I do not think any teaching would have made me a scratch golfer.

I have never consciously marked down a candidate either for his handwriting or his bad English, since he may make a very good doctor in spite of these drawbacks. I once failed to read an examination paper for a pass degree because the candidate wrote his words as much above as below the lines, and his paper looked like a series of small waves. I managed to decipher enough to realise that he was talking sense, and my co-examiner and those who read his other paper agreed to give him half marks, and let his fate be decided by the clinical and vivas. He passed very easily, and we requested that he be told that his handwriting was very bad, and that he ought to try to improve it.

I hope these confessions of a notoriously bad writer will support Sir John Conybeare's plea that bad writers should not be penalised, though they should be desired in the interests of the pharmacists and of their friends to write more legibly.

London, W.1. GEORGE GRAHAM

SIR,—As an examiner, I have never been unduly worried by the bad manners of the illegible candidate, but I have often been surprised by his stupidity. Harassed by an illegible script, I feel that I ought to deduct marks, but I never do—consciously, at least. Bad handwriting stamps a candidate as lacking in ordinary nous—a serious failing in any student who hopes to qualify as a doctor. However, until examiners as a whole agree on this, and warn candidates in advance that illegibility will be to their disadvantage, it is not fair for individual examiners here and there to exact penalties for bad handwriting (let alone crude spelling, or the inability to write a clear English sentence).

The illegible candidate is a fool to treat his poor examiner so. Let him envisage what happens to the scripts.

They arrive in two or three large parcels at the home of the examiner—who is almost without exception a kindly, sympathetic human being. They make a rather bulky-looking pile, to be marked in time, and (if there are many which are difficult to read) maybe against time. They probably remain on his desk until he gets home at the end of a day's work, has his dinner, and settles into an armchair in front of the fire. He starts with a sense of interested and, indeed, hopeful anticipation. Most candidates will not misunderstand me, however, when I add, with great respect, that examination scripts, in bulk, are not unduly inspiring reading. The examiner makes full allowance for this; but if by chance he comes upon a set of answers well and soundly set out in decent handwriting and readable English, he warms to the candidate, perhaps even a little excessively because of the contrast to the "general form."

Sooner or later comes the inevitable unreadable handwriting. The examiner stumbles on for a sentence or two, and then comes across a word which he cannot recognise. He turns the page through various angles in the effort to decipher it; he re-reads the previous sentences to see if they will lead him to the sense of the word; or he may even ask his wife's opinion (if, indeed, she has not already gone to bed). By the time it has been deciphered, he has probably forgotten what the candidate has said earlier. "Blast this chap," he mutters good-humouredly, "why wasn't he taught to write properly at school?" But he stumbles again, and again, and yet again, loses the thread of the argument, re-reads, and may even have to make notes on paper, to ensure that he will retain the candidate's meaning, and to assess whether he has covered the essentials of any proper answer to the question. The examiner, poor chap, has taken three or four times as long to go through this paper as through a normal one, with an altogether needless expenditure of energy. If he is as admirable as some of my friends who have contributed to this discussion,

he welcomes the extra labour involved as the opportunity to pay a debt; but most of us, I fancy, are very human, though we try to be humane. If there are several such scripts, we may even find the extra labour tiring.

At all events, I imagine that while most examiners on these occasions do in fact suffer fools, they do not suffer them gladly. It is a pity when a candidate forces an examiner to say to himself: "I must on no account let this prejudice me against this man; I must be fair, scrupulously fair." Fair he is, but a little warmth has gone out of the sky, and there is a chilly feel in the air.

Liverpool. ROBERT COOPE.

SIR,—After reading the views of two physicians (and examiners), a pharmacist, and finally a layman, I feel that an illegible candidate might himself express his opinion.

I do not feel that it is quite fair for examiners to penalise candidates for bad writing, as is proposed by the Royal College of Obstetricians and Gynæcologists. In the majority of medical examinations the spoken word in viva-voce and clinical examinations is, I am told, virtually the deciding factor in passing or failing many candidates. In view of this, could not bad writing be viewed with kindness by examiners, as Sir John Conybeare (May 16) and Professor Arnott (May 30) have suggested? I also feel that examiners in medicine are not put off by bad writing as much as examiners in other professions, because they do realise that the candidate often has great difficulty in selecting a few salient facts.

Finally, I would like to suggest to Mr. Playfair (June 13) that a candidate, in taking his finals in medicine, has little enough time for revision, let alone for changing his handwriting. XXX.

TRICHOMONAS VAGINITIS

SIR,—When I was an Army medical officer I was impressed with the higher incidence of amœbiasis in officers than in other ranks on one occasion when officers had the use of water-closets and other ranks did not. I wondered then whether splash contamination of the perineum on defæcation was a possible factor in the transmission of this disease.

I now suggest that splash contamination of the perineum may be a factor in the transmission of *Trichomonas vaginalis*. Risk of splash can be minimised by dropping a sheet of toilet-paper on the surface of the water in the lavatory pan before use.

London, N.10. J. L. PATTON.

TUBERCULOSIS IN GLASGOW

SIR,—In his letter last week Dr. James evades the issue, which is simply whether or not good housing and good nutrition are important factors in the campaign against tuberculosis. He admits that in the 100 years before 1947 the tuberculosis death-rate fell spectacularly. To what does he attribute this? Yadil?

Dr. James appears to claim that the reduction in Scandinavia is due to a high rate of hospital building, but what influence had hospital building on tuberculosis prior to 1947? Would Dr. James for a moment suggest that it was the *cure* of these patients in sanatoria which caused the reduction? Surely the generally accepted answer is that prior to 1947 what the hospitals did was to remove infected persons from their bad housing and put them in a position where they received adequate food. In other words, removal from bad housing and bad nutrition.

Dr. James and Northern Ireland are to be congratulated in that they have started to achieve from 1947 onwards by the use of antibiotics what we in this country had been achieving in the previous 20 years by attention to nutrition and housing.

Public Health Department, Smethwick. HUGH PAUL.

Obituary

ANDREW JOHN METFORD WRIGHT

M.B. Lond. and Brist., F.R.C.S.

Mr. John Wright, consulting surgeon to the ear, nose and throat department of the United Bristol Hospitals, died at his home at Clifton on June 11 at the age of 70.

He was born in Bristol, and he was rightly proud that his grandfather was William Budd, F.R.S., who did so much to demonstrate that infectious diseases are due to bacteria. He was educated at Blundell's School, Tiverton, and at the Bristol Medical School, qualifying in 1905. In 1907 he obtained the London M.B. with honours in medicine and surgery, and three years later he became F.R.C.S. He was appointed surgeon to the ear, nose, and throat department at the Bristol General Hospital in 1913, and he held this post until his retirement in 1946. He gave great service to his colleagues in the city by the immense interest he took in the Chesterfield Nursing Home. He spent much time there almost every day, caring for every detail of the running of the home.

He was a past president of the laryngological and of the otological sections of the Royal Society of Medicine, and in 1949 he was appointed to the Felix Semon lectureship of the University of London. Outside his professional work he had many interests and activities. At the outset of the first world war he was a combatant officer. From 1943 to 1952 he represented the Clifton ward on the Bristol City Council, and he took an active part in the work of the health committee. In 1948 he became chairman of the Cossham and Frenchay group of hospitals, and he had much to do with the organisation and equipment of Frenchay after the Americans left at the end of the late war. From 1945 to 1950 he was director of postgraduate studies in the University of Bristol.

A colleague writes: "Wright had a large private practice, and everyone knew that he could be relied on to give an honest, sensible, and well-informed opinion about his patients. On a committee he was in his element. His opinion was very likely to sway votes and carry the day. He would say afterwards, 'I poked a little fun at the proposition,' and that was apt to dispose of it altogether. He had a brand of dry humour that was all his own. That he had no enemies and hosts of friends was plainly shown by the large and representative company that attended the memorial service in Bristol Cathedral on June 16."

ALBERT EDWARD EVANS

C.B.E., M.B. Lond., D.P.H.

Dr. Edward Evans died on June 20, a few days before he was due to retire from his appointment as a Lord Chancellor's Visitor. His health had been impaired for some time, though a stranger meeting him would have been struck first and foremost by his cheerfulness as he went about his work or appeared, full of interest, at some medical symposium.

The son of Edward Evans, civil engineer, of Wrexham, he was born on June 29, 1881, and was educated at Llangollen County School, at Liverpool, and at University College Hospital. After qualifying in 1907 he held house-appointments at Stamford and was casualty medical officer at U.C.H. before taking a post as surgeon on a British India steamer. From 1909 to 1912 he was assistant medical officer at Rainhill Mental Hospital, and from 1912 to 1914 assistant M.O.H. for the county of Flint. He then became an inspector of the Board of Control, bringing to his duties a knowledge of Wales and of Welsh. But his work was soon interrupted by the outbreak of war in 1914. Joining the R.A.M.C. he reached the rank of lieut.-colonel, and he afterwards maintained his interest both in the Territorials and in hygiene by his visits to camp as medical officer to the Civil Service Rifles. In 1931 he was made a commissioner of the Board of Control, and in 1938 a Lord Chancellor's Visitor.

In his work at the board he interested himself particularly in infectious diseases and tuberculosis in mental hospitals, pointing out many years ago that tuberculosis in middle-aged and elderly people was commoner than had been supposed. He studied occupation therapy and encouraged its use. Another of his special interests was the treatment of patients, suffering from mental disorder or defect, in what were then public-assistance institutions. In 1948 he was appointed C.B.E.

I. G. H. W. writes: "To whatever he did Edward Evans brought a conscientious perseverance. It was entirely characteristic of him that, having taken up the organising of study-tours abroad for members of the Royal Medico-Psychological Association, he carried it on unobtrusively for twenty years, to the great benefit of psychiatry. But all his work was thorough. He regarded neither time nor comfort when he was occupied, and if a meal and a task came before him at the same moment it was the work which was done. His colleagues regarded him and his steady determination with great affection. He had a simplicity, a mischievous youthfulness, and a charm of manner that were not dimmed with the years. His friends who knew that he was not well can be glad that he had no wearisome decline to suffer, but died peacefully in his own home."

In his spare time Dr. Evans undertook many activities as a Freemason, and on holiday he was a keen fisherman with dry fly. His wife survives him.

HERBERT BERTRAM

M.B. Glasg.

Dr. Bertram, who died at Rotorua on April 15, at the age of 73, was a native of New Zealand, but he was proud of his Scottish ancestry, and it was to Glasgow University that he went, from Wanganui Collegiate School, for his medical education. After graduating in 1907 he returned to New Zealand, and the following year he started practice in Rotorua, the chief centre of that wonderland of subterranean thermal activity in North Island. Here he took an active part in public affairs and in the sporting and social activities of the town. He was a justice of the peace, and in 1922 he became a member of the first borough council. A keen sportsman and, in his day, a fine athlete, he was a foundation member of the Rotorua Hunt Club and was still its master at the time of his death. He had been president of the Rotorua Racing Club for 25 years, and he was a foundation member and former president of the local golf club.

M. J. S. writes: "Contemporaries of Bertram's Glasgow years retain a vivid memory of his athletic figure, handsome features, and attractive personality. Two years ago I had the good fortune to visit him and Mrs. Bertram in their delightful New Zealand home. I found him in great form, cheerful as ever, and carrying his years lightly. A very happy memory remains."

Dr. Bertram is survived by his wife, a son, and three daughters.

Dame GEORGIANA BULLER, D.B.E., R.R.C., who died at her home at Exeter on June 22 at the age of 69, will be remembered by many doctors for her work for the reablement of their patients. During the 1914–18 war, as organiser of the Exeter War Hospital she early realised the need not only to care for the wounded but also to give them a fresh start in life, and later her work was extended to include the casualties of industry. She was one of the founders of St. Loyes College for Training and Rehabilitation of the Disabled and of the Queen Elizabeth's Training College for the Disabled at Leatherhead, and for many years she was chairman of both these bodies. She was also a vice-chairman of the British Council for Rehabilitation.

Births, Marriages, and Deaths

BIRTHS

KHOSLA.—On May 31, at West Middlesex Hospital, Isleworth, to Saroj, wife of Dr. H. Khosla—a son (Rajiv).

Notes and News

REQUIREMENTS FOR THE D.P.M.

THE Psychological Medicine Committee of the Royal College of Physicians has been considering the existing regulations for the diploma in psychological medicine, and some of its recommendations have now been approved by comitia.

The content of the examination will not be altered, but the new requirements will be less inconvenient to fulfil. The present regulations may oblige candidates to change their residence in order to get the necessary experience, and this can cause real hardship to married men whose earnings are small. Moreover, because of National Service, those taking the D.P.M. are older than their forerunners, and thus more likely to be discouraged by such difficulties. The committee felt, too, that the present regulations throw disproportionate emphasis on certain aspects of psychiatry.

No useful purpose, the committee thought, is served by detailed regulations as to the way the candidate gets his experience: candidates for the M.R.C.P. are not asked to spend a definite period of study on cardiac or thoracic medicine. The D.P.M. examination itself ought to be an adequate test of the knowledge required, and should represent fair competence and fair experience in the successful candidate—such as should be within the range of the average doctor working in a mental hospital who may not aspire to consultant status.

Under the new regulations the candidate will be asked to produce evidence of two years' experience in a recognised psychiatric hospital, centre, or department. The criteria for recognition of a mental hospital are that it should have a formal liaison with a general hospital, an outpatient department, consultants on its staff in other branches of medicine, regular clinical case-conferences at least once a week, access to a department of clinical psychology, a medical library, and at least two psychiatric consultants on the staff. Normally all mental hospitals, neurosis hospitals, and psychiatric departments of teaching hospitals will be recognised. Not more than twelve months of the two years should be spent by the candidate in a hospital or department without psychiatric beds. The amount of experience in neurology, mental deficiency, or child psychiatry required of a candidate will not be laid down; but the examination in neurology will stand, and the candidate will also be required to show knowledge of mental deficiency, child psychiatry, forensic psychiatry, and social psychiatry. The committee added that, in order that candidates might acquire the special experience they need, they should be given adequate time off from routine duties.

Superintendents of mental hospitals will be glad to know that the regulations have been modified in this way.

SAVING MONEY ON HOSPITAL LAUNDRIES

IN Scotland the Western Regional Hospital Board, aware that money could be saved by rationalising and centralising hospital laundries, engaged the British Launderers' Research Association to survey the resources. The board has accepted the association's recommendations, slightly modified to suit local conditions. Twenty-six hospital laundries have been selected as potential centres, while nineteen others are to be retained for the use of the parent hospitals only. Fifty-three laundries are to be closed. Work now sent to commercial laundries from forty-six hospitals is to be transferred to the proposed central laundries. The cost of capital development in connection with this scheme is estimated at about £150,000; but it is expected that the saving on annual expenditure will eventually amount to £50,000–£60,000.

AMBULANCE SERVICES

THE Ambulance Services Costing Return[1] for the year ended March 31, 1952, shows that both the mileage and the number of patients carried were greater than in the previous year. The figures are:

Year	*Patients*	*Mileage*
1950–51	9,000,000	89,000,000
1951–52	11,000,000	92,000,000

For this return a patient is defined as "one patient carried once in one direction; and the increase in the number of patients carried may be less than the return suggests since

1. National Health Service: Ambulance Services Costing Return, 1951–52. H.M. Stationery Office. Pp. 24. 3s.

up to 1951–52 some authorities were counting only once outpatients carried in both directions. The average number of miles run per patient has fallen from 9 to 8·3, and the average cost per patient from 15*s.* 6*d.* to 15*s.* 2*d.* The total cost of the ambulance services in the year was £8,608,828.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

AT the annual meeting of this society on June 18, Sir Neil Hamilton Fairley, F.R.S., the retiring president, inducted the new president, Dr. F. Norman White. Dr. White presented the Manson medal, which is awarded every three years for distinguished service to tropical medicine, to Prof. Jérôme Rodhain (Antwerp). Dr. White also presented the Chalmers medal to Mr. D. J. Lewis, entomologist, of the Sudan Medical Service.

MEDICAL SICKNESS SOCIETY

AT the annual meeting of the Medical Sickness, Annuity, and Life Assurance Society on June 16, Mr. R. J. McNeill Love, the chairman, observed that the combined funds now exceeded £5 million, compared with £1 million less than twenty years ago. The membership had risen to just over 14,000. Dr. T. C. Hunt has been appointed medical officer in succession to Dr. A. Hope Gosse, who has retired from this post after holding it for twenty-seven years.

UNIVERSITIES OF THE COMMONWEALTH

THE 30th edition of the *Commonwealth Universities Yearbook*[1] once more gives all the information which its title promises. The editor happily takes the view that "despite certain present-day colloquial usages the term 'Commonwealth' does include the United Kingdom," and a third of its pages is given to the universities which lie nearest London. Even universities of the Republic of Ireland are tactfully included in a useful if unconstitutional appendix. The world of learning continues to expand and this edition includes five new universities—three in India, one in Pakistan, and one in England (at Southampton). Its index contains 30,000 names. This new edition has been timed to appear before the seventh quinquennial congress of the Universities of the Commonwealth at Cambridge this summer. Its first readers will probably be the delegates to that gathering, but many other academic workers all over the world will value it as a handy reference book.

ANTHROPOLOGICAL SOLUTIONS FOR PATERNITY PROBLEMS

UNTIL quite recently the only biological test accepted by law in Sweden for determining disputed parenthood depended on blood-grouping. A new law, however, which came into force in 1950, accepts certain genetic characters as complementary evidence in paternity cases. Dr. Jan A. Böök,[2] of the Swedish State Institute for Human Genetics at Uppsala, admits that most paternity cases still have to be left undecided by genetic tests. But in 10–15% of the cases referred by the law-courts, the institute has been able to furnish useful information. One example cited by Dr. Böök is a case in which blood-grouping tests had failed to show whether K or P was the father of the child in question. The child and P were brown-eyed, whereas the mother and K were blue-eyed, without a trace of brown pigment in the iris. At the Uppsala Institute no brown-eyed offspring have hitherto been traced to parents who were both strictly blue-eyed. P and the child had finger-prints whose pattern did not occur in either the mother or K. The muscles of the ears of the child and P were more alike than were those of the child and mother, while K had a quite different type of ear. The child and P had remarkably similar nails, whereas in the mother and K the nails were of a different type. Radiographic examination showed narrow, undeveloped twelfth ribs in the mother and P, while the child had no twelfth ribs whatever; in K the ribs were normally developed. On the strength of these findings K was absolved from the parentage of the child with a probability amounting to certainty. It was also ruled that P was probably the father. In Dr. Böök's opinion anthropological paternity tests are not satisfactorily applicable to children less than 2 years old.

1. The Yearbook of the Universities of the Commonwealth, 1953, London: published for the Association of Universities of the British Commonwealth by G. Bell & Sons. 1953. Pp. 1805. 63*s.*
2. *Nord. Med.* May 22, 1953, p. 735.

TRANSPLANTATION BULLETIN

A QUARTERLY *Transplantation Bulletin* is to be produced in the U.S.A., with Dr. Herbert Conway, Dr. Ernest J. Eichwald, and Mr. Nathan Kaliss, PH.D., as managing editors, and Dr. Blair O. Rogers as associate editor. The functions of the bulletin will include the maintenance and publication of a "transplantation registry" listing physicians and research-workers in the U.S.A. and elsewhere who are interested in transplantation problems. It will also provide for rapid and informal exchange of information, attempt to keep members of the registry informed of relevant forthcoming meetings, and maintain bibliographies. Those interested are asked to submit their name and field of interest to Dr. Eichwald, University of Utah College of Medicine, Salt Lake City, Utah. A subscription of $3 will be payable after the first issue of the bulletin has been published. This issue is expected to appear in August.

LIGHT-WEIGHT CRUTCHES

FOR 'Airleg' crutches the manufacturers[1] claim two advantages: first, that the axillary support is comfortable because it is covered with an inflatable rubber sleeve; and secondly, that both the length of the crutch and the position of the handle are easily adjustable over a large range by a single manœuvre. Trial proves these claims to be well founded. The crutch is solidly constructed of light metal and appears to be durable. No information is available as to how long the inflatable sleeves will last, but they are replaceable. The price of the crutches (£4 10*s.* per pair) is greater than that of the standard hospital type; but their convenience in so far as only two sizes are required (for adults and for children), comfort, and durability would make them a paying proposition were it not that crutches are lost to hospitals not so much through breakage as through failure by patients to return them. In one hospital 278 pairs are on issue at present; the return of over 200 is overdue, and nearly three-quarters of this number are retained by patients to whom the hospital authorities have already written twice or more asking for their return. It is true that patients are made to sign for their crutches and under the National Health Service Act are liable for their value; but the cost and trouble of the necessary litigation would make the game of re-claiming them scarcely worth the candle.

THE RAT

AUDIENCES in London have lately seen a group of five films made by the Rodent Research Station of the Quarantine Branch of the United States Public Health Service. These were shown first at the London School of Hygiene and Tropical Medicine by the medical officer of health for the Port of London (Dr. M. T. Morgan), and later, on June 11, by the Royal Sanitary Institute.

The titles of the films (The Rat Problem; The Roof Rat; The Norway Rat; Rat-proofing; and Rat-killing) indicate their scope. In a natural urban setting, the full range of normal rat activities is displayed without hurry. Rats are seen being born, growing, climbing, exploring, eating, drinking, fighting, and mating. From birth to death the rat is observed, without omission or exaggeration. In one scene a rat is shown attacking and killing a young chicken; in another, a fight between two varieties of *Rattus rattus* adds excitement to instruction. The running commentary explains the importance of understanding the rat's habits and habitats if we are to encompass his destruction.

One film shows how buildings should be "proofed" and how rodenticide chemicals and traps are used. A simple and ingenious control measure to demonstrate survivors' footmarks is well illustrated. The preparation and use of red squill, arsenic trioxide, and 'Warfarin' are displayed in detail.

When it is recalled that, apart from their responsibility for spreading disease, rats and mice account for an estimated annual destruction of some 2 million tons of foodstuffs in Great Britain, and that the loss of wheat through their activities costs us £30 to £40 million a year, a fresh stimulus to their control is valuable.

University of Leeds

Mr. M. Ellis has been appointed clinical lecturer in surgery, and Mr. B. Farquhar clinical lecturer in obstetrics and gynæcology.

1. Light Alloy Utilities Ltd., Prince of Wales Road, Norwich.

University of Sheffield

Dr. A. J. N. Warrack has been appointed honorary part-time lecturer in pathology.

Royal College of Surgeons in Ireland

On June 18 the fellowship of the college was conferred on the following:

A. J. C. Allison, S. C. Baker, P. G. Brady, M. B. O'Donnell.

On Oct. 8 the president, vice-president, and council will elect a part-time professor of surgery. Terms of appointment can be had from the registrar of the college, St. Stephen's Green, Dublin. Applications must be submitted by Aug. 17.

Irish Conjoint Board

At recent examinations of the Irish Conjoint Board the following were successful:

D.A.—P. R. Mesham, T. W. Vanniasingham, N. H. Jafry, Mary L. Mackay, Evelyn M. Gallagher, J. R. McCarthy, M. F. McGrath, E. A. Vaughan, J. D. Carstens, Nora M. Kelleher, A. A. Alvarez, J. D. Twomey, P. M. F. McGarry.

D.C.H.—J. K. Heskin, Joan M. MacCarthy, J. F. O'Halloran, H. Z. G. O. Senanayake, Hirarani Thakur, T. J. Mahon, T. J. M. Lydon, Geeta S. Mehta.

D.O.M.S.—H. J. Scott.

London College of Osteopathy

A postgraduate course for registered medical practitioners will begin in October. Particulars may be had from the secretary of the college, 25, Dorset Square, N.W.1.

Conference on Military Medicine

The next session of the Office International de Documentation de Médecine Militaire will be held in Rome, from Oct. 14 to 18. Further particulars may be had from Colonel Médecin A. Campana, Ministero della Difesa-Esercito, Rome.

Conference on Medical Photography

The fourth annual conference of the medical group of the Institute of British Photographers will be held at the University of Leeds, from Sept. 25 to 27. The speakers will include Prof. R. E. Tunbridge, Dr. C. W. Dixon, and Dr. P. N. Cardew. Further details and tickets can be had from Miss C. E. Campbell, department of medical photography, St. James's Hospital, Leeds, 9.

A Roll of Health-visitor Tutors

For the guidance of local authorities and other bodies responsible for the appointment of tutors in health-visitor training centres and with a view to emphasising the need for a high standard of qualification among such tutors, the Royal College of Nursing, at the request of the Standing Conference of Representatives of Health Visitor Training Centres approved by the Ministry of Health, has agreed to set up a roll of health-visitor tutors. Applicants must either hold the health-visitor tutor certificate of the college or have had such practical and teaching experience as the council of the college may deem adequate.

British Standard for Hæmocytometers

A revised British standard for hæmocytometer counting-chambers and hæmocytometer dilution pipettes has been issued (B.S.748/1953).

As in the original 1937 edition, requirements are specified for counting chambers with single or double rulings, and for dilution pipettes suitable for dilutions of 1 in 100 and 1 in 10. To the Neubauer and Bürker rulings previously specified have been added the improved Neubauer and Fuchs Rosenthal rulings. Dimensions and tolerances are given for the slides, rulings, and coverglasses, and inscriptions for the slides. The material, construction, dimensions, graduation, and inscriptions for the pipettes are specified, and also the definition and tolerances for the dilution-ratio.

Copies of this standard (3*s.* 6*d.*) may be obtained from the British Standards Institution, Sales Branch, 24, Victoria Street, London, S.W.1.

CORRIGENDA: *Journal of the American Geriatric Society.*—This journal is published monthly, and not bi-monthly as was stated in our annotation of April 18 (p. 781).

Transplantation of Human Tumours.—In Dr. F. C. Chesterman's letter last week (p. 1253) the third line of the third paragraph should begin with the words: "inhibit the host reaction to the implant."

What is Ulcerative Colitis?—In fig. 3 of Mr. B. N. Brooke's article last week (p. 1220), the caption should have read "Ileocolitis," and *not* "True 'idiopathic' ulcerative colitis."

Diary of the Week

JUNE 28 TO JULY 4

Monday, 29th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. F. Stansfield: Paranasal Sinuses. (Arnott demonstration.)

UNIVERSITY COLLEGE, Gower Street, W.C.1
5 P.M. Dr. Warren S. McCulloch (Massachusetts Institute of Technology): New Techniques for Electrophysiological Study of Central Nervous System.

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Colonel W. R. M. Drew: Recognition and Treatment of Dysentery.

Tuesday, 30th

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. R. J. Last: Knee-joint. (Arnott demonstration.)

INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr. A. R. French: Medicolegal Problems and the Dermatologist.

Wednesday, 1st

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. E. F. Gale: Mode of Action of Antibacterial Agents. (Second of two lectures.)

UNIVERSITY OF OXFORD
5 P.M. (University Museum.) Prof. Wilder Penfield, O.M., F.R.S.: The Learning of Languages.

YORKSHIRE SOCIETY OF ANÆSTHETISTS
8 P.M. (General Infirmary, Leeds.) Dr. T. C. Gray, Dr. J. W. Dundee, Mr. H. F. V. Riddle: Facts about Dosage.

Thursday, 2nd

ROYAL COLLEGE OF SURGEONS
5.30 P.M. Sir Henry Dale, O.M., F.R.S.: Histamine and its Antagonists. (Otolaryngology lecture.)

INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1
5 P.M. Prof. G. Fanconi (Zürich): Renal Dwarfism.

EMPIRE RHEUMATISM COUNCIL
8.15 P.M. (1, Wimpole Street, W.1.) Sir Henry Cohen: Concept of Collagen Disease. (Coronation lecture.)

UNIVERSITY OF OXFORD
5 P.M. (Radcliffe Infirmary, Oxford.) Prof. W. B. Castle (Harvard University): Speculations about the Cause of Polycythæmia Vera.

Friday, 3rd

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5 P.M. Dr. McCulloch: Cerebral Control of Carbohydrate Metabolism.

Appointments

COUPER, LEWIS, M.B. Glasg., D.P.M.: whole-time deputy medical superintendent (consultant), Winwick Hospital.

FRASER, ANDREW, M.B., B.SC. Glasg., D.A.: consultant anæsthetist, Hartlepools H.M.C. group.

NUTT, RONALD, M.R.C.S.: appointed factory doctor, Godalming district, Surrey.

OLLIFF, D. E., M.B. Brist.: appointed factory doctor, Chipping Campden, Gloucestershire.

ROWLANDS, DAVID, M.R.C.S.: consultant anæsthetist, Clwyd and Deeside, and the Caernarvon and Anglesey H.M.C. areas.

WINTER, JOHN, M.B., M.RAD. Lpool, D.M.R.D.: consultant radiologist, N. Liverpool and Fazakerley groups of hospitals.

Leeds Regional Hospital Board:

EDWARDS, G. F., M.B.E., M.B. Lond., M.R.C.P.: senior consultant chest physician, Leeds chest clinic.

PENHEAROW, R. M. B., M.B. Madras: asst. anæsthetist (S.H.M.O.), Wakefield A and B groups.

ROBERTSON, STRUAN, M.B. Edin., D.O.M.S.: whole-time ophthalmologist (S.H.M.O.), Bradford and Halifax areas.

WINCHESTER, GEORGE, M.B. Edin., F.R.C.S.E., M.R.C.O.G.: part-time consultant in obstetrics and gynæcology, Hull and East Riding groups.

The Hospital for Sick Children, Great Ormond Street, London:

ECKSTEIN, H. B., M.A., M.B. Camb.: house-surgeon.

HEYWOOD, T. J., M.D.: house-physician.

JACO, N. T., B.M. Oxfd, M.R.C.P., D.C.H.: asst. medical registrar.

MARTIN, ELIZABETH, M.B. Lond.: house-physician.

MILLARD, A. H., M.B. Lond., F.R.C.S.: surgical registrar.

TILL, KENNETH, M.A., M.B. Camb.: clinical asst., neurosurgical department.

WILKINSON, J. A., M.B. Wales: house-surgeon.

WILLIAMS, M. R., B.M. Oxfd, F.R.C.S.: part-time surgical registrar.

University College Hospital of the West Indies, Jamaica:

FORD-SMITH, JOYCE, M.B. Aberd., D.OBST.: lecturer in obstetrics and gynæcology.

HOYTE, H. A. ST. C., M.D. McGill, D.OBST.: registrar in obstetrics and gynæcology.

PINKERTON, J. H. M., M.D. Belf., M.R.C.O.G.: senior lecturer in obstetrics and gynæcology.

SELF, J. B., M.A., M.B. Camb., F.R.C.S.: surgical registrar.